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THE ELECTRO-ENCEPHALOGRAM IN EPILEPSY AND IN CONDITIONS OF IMPAIRED CONSCIOUSNESS

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The electro-encephalogram is the graphic record of electrical disturbances arising in the brain. This record is analogous to the electrocardiogram, which is the record of the electrical action current associated with the contraction of the heart. The first systematic study of electro-encephalograms of human beings was carried out by Berger in the years following 1929.[1] He established the cerebral origin of these electrical potentials, classified them according to frequency and amplitude and determined the conditions of their appearance and disappearance. He showed further that it was possible to record these phenomena from the intact skull of the conscious human subject. Adrian [2] also investigated these cortical potentials in both man and animals, and numerous other investigators, including Foerster and Altenburger,[3] have added significant contributions.

Our interest in the subject was aroused by the work of Berger and by the realization that in our electrical amplifiers and oscillographs we

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1. Berger, H.: (*a*) Ueber das Elektrenkephalogramm des Menschen, Arch. f. Psychiat. **87**:527, 1929; (*b*) Ueber das Elektrenkephalogramm des Menschen, ibid. **99**:555, 1933; (*c*) Ueber das Elektrenkephalogramm des Menschen, ibid. **97**:6, 1932; (*d*) Ueber das Elektrenkephalogramm des Menschen, ibid. **98**:231, 1933; (*e*) Ueber das Elktrenkephalogramm des Menschen, ibid. **100**:301, 1933.

2. (*a*) Adrian, E. D., and Matthews, B. H. C.: The Interpretation of Potential Waves in the Cortex, J. Physiol. **81**:440, 1934. (*b*) Adrian, E. D.: Electrical Activity of the Nervous System, Arch. Neurol. & Psychiat. **32**:1125 (Dec.) 1934. (*c*) Adrian, E. D., and Matthews, B. H. C.: The Berger Rhythm: Potential Changes from the Occipital Lobes in Man, Brain **57**:355, 1934.

3. Foerster, O., and Altenburger, H.: Elektrobiologische Vorgänge an der menschlichen Hirnrinde, Deutsche Ztschr. f. Nervenh. **135**:277, 1935.

possessed a promising instrument with which to attack certain difficult problems of neurology. Two of us were already particularly conversant with the problem of epilepsy, and we therefore undertook to use our electrical technic in a search for the neurologic basis of this disorder.

METHOD

The method is exceedingly simple. Electrical contact is made to two points on the subject's head. Except for the study of grand mal epileptic seizures we regularly employ as electrodes two hypodermic needles inserted one into the scalp at the vertex of the skull and the other into the lobe of the left ear. Enough procaine hydrochloride is injected previously to insure the continued comfort of the subject. External electrodes in the form of pads or plates are used by Adrian and Matthews [4] and by Jasper and Carmichael,[5] but we are inclined to agree with Berger that ordinarily needle electrodes are more convenient for long continued observations and generate fewer extraneous potentials as a result of slight mechanical movements. Electrodes in our positions are not affected by the electrocardiogram or by the action potentials generated in most of the skeletal muscles. Such activities as clenching the teeth, wrinkling the brow or vigorous swallowing may affect the record, but these disturbances may be easily distinguished by their sharp and rapid fluctuations which differ characteristically from the cerebral potentials (chart 5). If they are not too powerful, these extraneous waves may be filtered out to a considerable extent by using a low frequency recording instrument such as we are about to describe. Such filtering is a great practical convenience.

For the study of grand mal epileptic seizures, in order to avoid as far as possible muscle action potentials, we used a diffuse ground electrode, in the form of a crown, made of wire and wrapped with cotton soaked in salt solution. This ring or crown electrode was adjustable in diameter and could be fastened tightly around the patient's head. A needle electrode in the scalp at the vertex of the head was used, as in other cases, for the grid lead. With these leads, despite generalized motor activity involving the jaw, eyes and face, very little in the way of muscle action potentials was obtained. The only muscle action potentials that were in the least troublesome came from the upper part of the frontalis muscle, and these were so small that with the low amplification required for recording convulsions they did not show in the record. Apart from the elimination of the action potentials of the muscles, these leads yield records identical with those obtained from our standard leads.

If a very sensitive recording instrument, such as a good string galvanometer with slack string, is connected directly to the electrodes in a normal subject, an electro-encephalogram may be obtained. The changes in potential, however, which may be led off from the head are usually not greater than from 10 to 50 microvolts, about one hundredth of the voltage available for the electrocardiogram. Practical considerations usually make it necessary, therefore, to resort to electrical amplification. If this is done, one may select a recording instrument with a view to convenience and cheapness instead of being bound by the requirements of

4. Adrian and Matthews [2b,c]

5. Jasper, H. H., and Carmichael, L.: Electrical Potentials from the Intact Human Brain, Science **81**:51, 1935.

extreme sensitivity. For our recording instrument we have employed an ink-writing oscillograph, known as the "undulator," obtained from the Western Union Telegraph Company. With certain modifications [6] it is satisfactory for recording signals up to a frequency of about 40 per second. The record is written directly on a paper tape, and because of the cheapness of operation it is perfectly practical to take continuous records over a period of many hours. This is a great advantage in studying patients with occasional epileptic seizures and in investigating modifications of the electro-encephalogram during sleep. Another advantage of this type of record is its immediate visibility, in contrast to photographic records, which cannot be studied until after development. The most serious limitation is its failure to deal effectively with frequencies above 40 per second, but we have compared the performance of this instrument with simultaneous records made with a cathode ray oscillograph and have assured ourselves that below this limiting frequency our ink-writing oscillograph gives an essentially faithful record of the phenomena which we shall describe.

The amplifiers with which most of our observations have been made are those which have already been in use in this laboratory for several years in the study of the electrical phenomena of audition.[7] The principle of an ink-writing oscillograph is not new. A similar instrument was described by Toennies,[8] and another form has been employed by Adrian and Matthews.[9]

THE NORMAL ELECTRO-ENCEPHALOGRAM

If a normal subject with electrodes applied to his head sits relaxed with eyes closed, an electro-encephalogram is obtained which is characteristic for himself but which may differ considerably from the record of another person. In general, however, all such records have certain basic features in common. The most prominent waves have a frequency between 8 and 20 per second and a total voltage, measured from trough to peak, of from 10 to 50 microvolts. The pattern may change in detail from moment to moment, but its general appearance is characteristic of the individual subject. The records are not greatly altered by shifting the position of the active electrode, which is usually placed at the vertex of the skull. This is in general agreement with Berger's observations [10] and also with those of Foerster and Altenburger,[3] who made contact directly with the brain during surgical operations. Differences in detail

6. Garceau, E. L., and Davis, H.: An Ink-Writing Electro-encephalograph, Arch. Neurol. & Psychiat, this issue, p. 1292.

7. Garceau, E. L., and Davis, H.: An Amplifier, Recording System, and Stimulating Devices for the Study of Cerebral Action Currents, Am. J. Physiol. **107**:305, 1934.

8. Toennies, J. F.: Der Neurograph, ein Apparat zur unmittelbar sichtbaren Registrierung bioelektrischer Erscheinungen, Deutsche Ztschr. f. Nervenh. **130**:60, 1933.

9. Adrian and Matthews.[2c]

10. Berger.[1b]

do appear, however, as one might expect from the observations by Kornmueller [11] of characteristically different records obtained by making direct contact with various regions of the brains of animals. These differences fall within the general characteristics which we describe.

We have selected the vertex of the skull as the standard location for the active electrode because of the absence of underlying musculature and because of the proximity of the motor cortex. In comparing our results with those of other investigators the position of the electrodes must be considered, as the picture may differ in certain respects with electrodes in different positions. We have studied an arbitrary sample of the electrical activity of the brain and do not claim that the phenomena which we observe are necessarily associated with the motor areas alone, on the one hand, or with the entire brain, on the other hand. We do not know whether the potentials we lead off come from the region of the motor cortex alone or from some other part of the brain as well. The question of which leads are best can be answered only after much more experimentation. The standard locations we have used have, from our point of view, one great practical advantage—they give a phenomenon which alters definitely and characteristically with certain disturbances of consciousness and with epileptic seizures.

Berger called particular attention to what he calls α waves. These are relatively large and quite regular and occur at a frequency of about 10 per second. Adrian confirmed Berger in this description. What Berger has called α waves and Adrian has called "the Berger rhythm" seem to be most closely connected with the part of the brain concerned with visual function. Some subjects show this rhythm with great clearness and regularity; others show it only occasionally, while still others show it scarcely at all. The most favorable conditions for its appearance are mental and physical relaxation and closure of the eyes. It is most effectively abolished by opening the eyes. Adrian attributed its disappearance primarily to activity of the visual apparatus.[9] Berger expressed the belief that any effort of the "attention" leads to the disappearance of his α waves. On the whole, we agree with these generalizations, but in the case of one epileptic patient we have seen a

11. Kornmueller, A. E.: (*a*) Bioelektrische Charakteristika architektonischer Felder der Grosshirnrinde, Psychiat.-neurol. Wchnschr. **34**:25, 1932; (*b*) Architektonische Lokalisation bioelektrischer Erscheinungen auf der Grosshirnrinde: Untersuchungen am Kaninchen bei Augenbelichtung, J. f. Psychol. u. Neurol. **44**:447, 1932; Bioelektrische Erscheinungen architektonischer Felder: Eine Methode der Lokalisation auf der Grosshirnrinde, Deutsche Ztschr. f. Nervenh. **130**:44, 1933; (*c*) Die Ableitung bioelektrischer Effekte architektonischer Rindenfelder vom uneroeffneten Schaedel, J. f. Psychol. u. Neurol. **45**:172, 1933; (*d*) Die bioelektrischen Erscheinungen der Grosshirnrinde, Fortschr. d. Neurol., Psychiat. **5**:419, 1933.

strong 10 per second rhythm remain unaltered when he opened his eyes and read an unfamiliar sign in small print, which certainly required both vision and attention. It disappeared, however, when the subject was spoken to. In normal persons we have frequently produced a flattening of the record after sudden auditory stimulation, as with a watchman's rattle (chart 1). The same stimulation a few minutes later usually causes less change or even no change at all, while in another subject it may introduce new waves of increased amplitude and slower frequency (chart 1). Some persons show these reactions more readily than others. These observations illustrate how the effect of a given

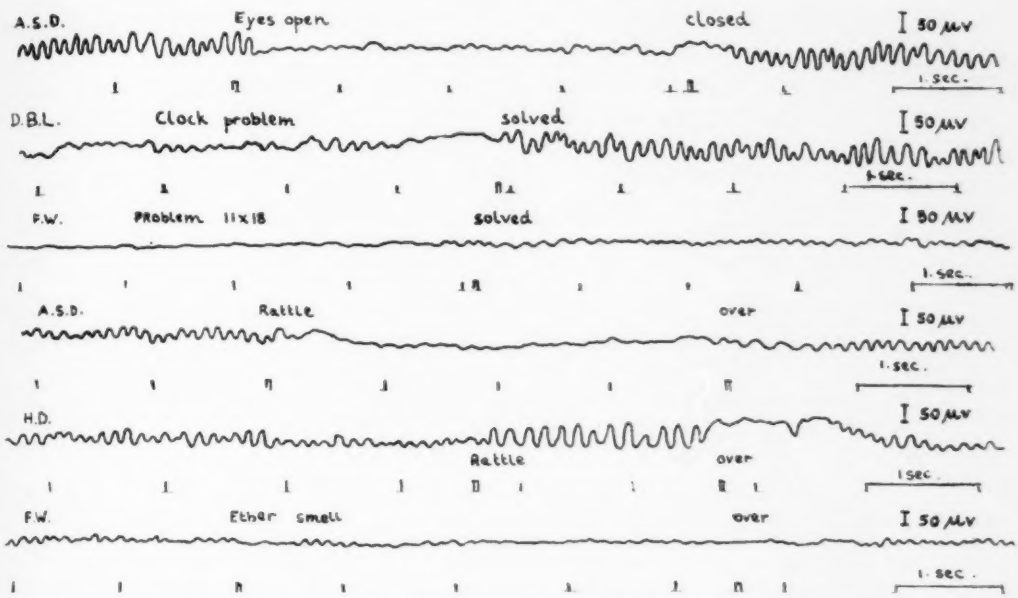

Chart 1.—Alterations in the electro-encephalograms of normal subjects produced by sensory stimulation and by mental effort. These strips are taken from the records of various subjects. The length of the *I* at the upper right margin on each strip indicates the deflection produced by a 50 microvolt signal. The vertex becoming electrically negative to the ear gives an upward deflection. The vertical lines on the lower edge of the strips give the time in seconds. In the record marked *A.S.D.* the subject was sitting quietly with the eyes closed in a well illuminated room when, on command, he opened and then closed his eyes. In the record marked *D.B.L.* the subject, while sitting with eyes closed, was asked to tell the angle of the hands of a clock when the hands point to fifteen minutes after ten. The strip begins while the subject was struggling with this problem; the record is much flattened and returns to its previous form only as the problem is solved. In the record marked *F.W.* the subject was asked while sitting with eyes closed to multiply 11 by 18. This strip also begins while the subject was working on the problem and shows the same flatness with a return to normal activity as the problem is solved. In records marked *A.S.D.* and *H.D.* a loud noise was made with a watchman's rattle. The subject's eyes were closed throughout.

sensory stimulation may differ from person to person and from time to time.

In most of our subjects, concentrated mental activity, such as the performance of "mental arithmetic" or the attempt to form a clear mental image, produces a more or less definite flattening of the record (chart 1).

SLEEP

We have obtained electro-encephalograms during sleep from thirteen subjects who were normal in respect to sleep and from four persons

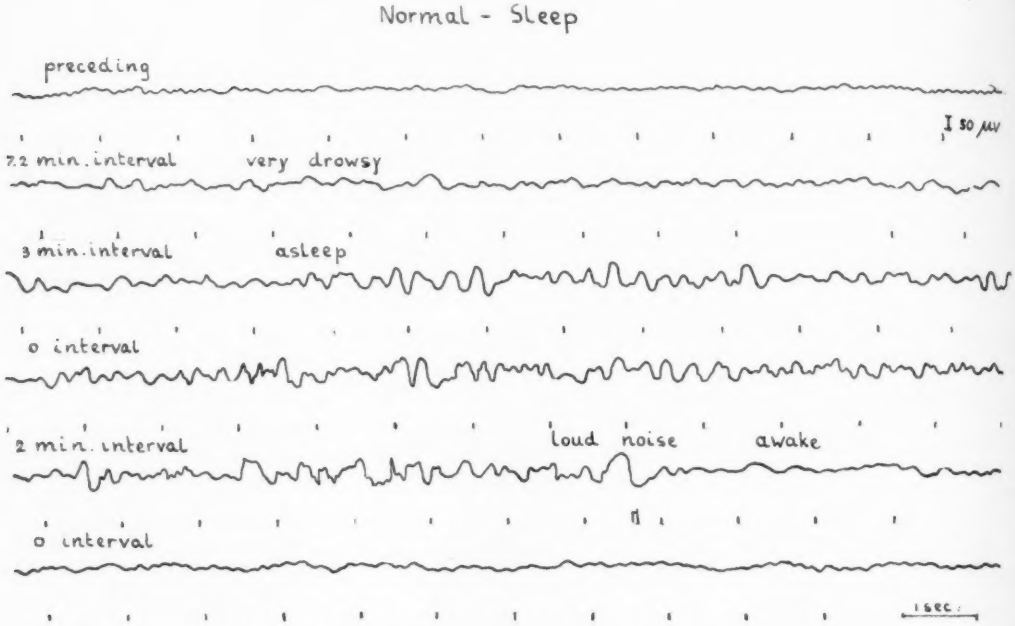

Chart 2.—Alteration of the electro-encephalogram with normal sleep. The increase in amplitude and decrease in frequency of the waves while the subject was asleep are obvious, as is the tendency for waves to appear in bursts. The height of the *I* at the end of the first strip indicates the deflection produced by a 50 microvolt signal. The vertex becoming electrically negative to the ear gives an upward deflection. The vertical lines at the bottom of the strips give the time in seconds. A loud noise was produced by the experimenter clapping his hands.

with narcolepsy. In all cases, as the subject becomes very drowsy the predominant waves become slower and show a greater amplitude. If a strong Berger rhythm is present, it may first diminish, leaving a less intense and more irregular activity in evidence. As the subject falls sound asleep, however, the predominant electrical activity becomes still slower and smoother, showing a characteristic frequency of from

3 to 5 per second. The voltage has now increased to about 60 microvolts. Faster waves reappear after a longer or shorter interval and usually show a larger amplitude and somewhat slower frequency than is characteristic of that person's waking record.

The reappearance of the faster waves is sometimes definitely periodic. It occurred every fifteen seconds in one case and every forty seconds in another. As these bursts of activity occur, the subject sometimes gives a restless movement or a jerk. When the subject awakens or is awakened, the normal waves reappear promptly, usually after a transient burst of larger, slightly slower waves than normal (chart 2).

Berger reported that in sleep the α waves decrease in amplitude.[12] We do not use Berger's term, "α waves," as we prefer to characterize the waves by frequency and voltage until definite functional attributes can be determined. This seems all the more desirable as it seems likely that we are dealing with a continuous range of amplitude and of frequency rather than with discrete classes. We have not attempted to observe in detail Berger's β waves of 50 or 60 per second, but are confining this description to the slower and larger components.

In summary, we can say definitely that the character of the electro-encephalogram alters in sleep and that persons who when awake with eyes closed show a pronounced 10 per second rhythm show much less of this rhythm during sleep. On the other hand, some of the largest waves we have seen in normal persons occur during sleep. Berger's description of the change as being in the direction of a flattening of the record is apparently incomplete.

PETIT MAL EPILEPSY

Electro-encephalograms from twelve patients[12a] with characteristic petit mal epilepsy show in all cases during the seizure an outburst of waves of great amplitude, amounting to from 100 to 300 microvolts at a frequency of 3 per second. These waves may be very smooth and approximately sinusoidal in shape but usually include a sharp negative spike breaking into the record near the positive crest of the main wave (chart 3). The large 3 per second wave is invariably present. The spike is more variable in amplitude and may occasionally be absent during part of a seizure. Records from the same subject in successive seizures tend to be closely similar to one another.

The electro-encephalograms of these epileptic patients made between seizures are essentially normal, except that scattered here and there are brief groups of waves of pattern similar to those seen at the beginning of a seizure. The voltage is lower than in a well developed outburst,

12. Berger.[1c]

12a. The patients now, at the time proof of the article was read, number thirty-four.

however, and the characteristic pattern is less marked. These we have called "larval" seizures, because they so closely resemble the beginning of a fully developed characteristic seizure but fade out again instead of developing the characteristic picture.

The twelve patients studied showed several varieties of petit mal seizure. Some had slight motor involvement and some almost none. The records, nevertheless, are all strikingly similar. The presence of the

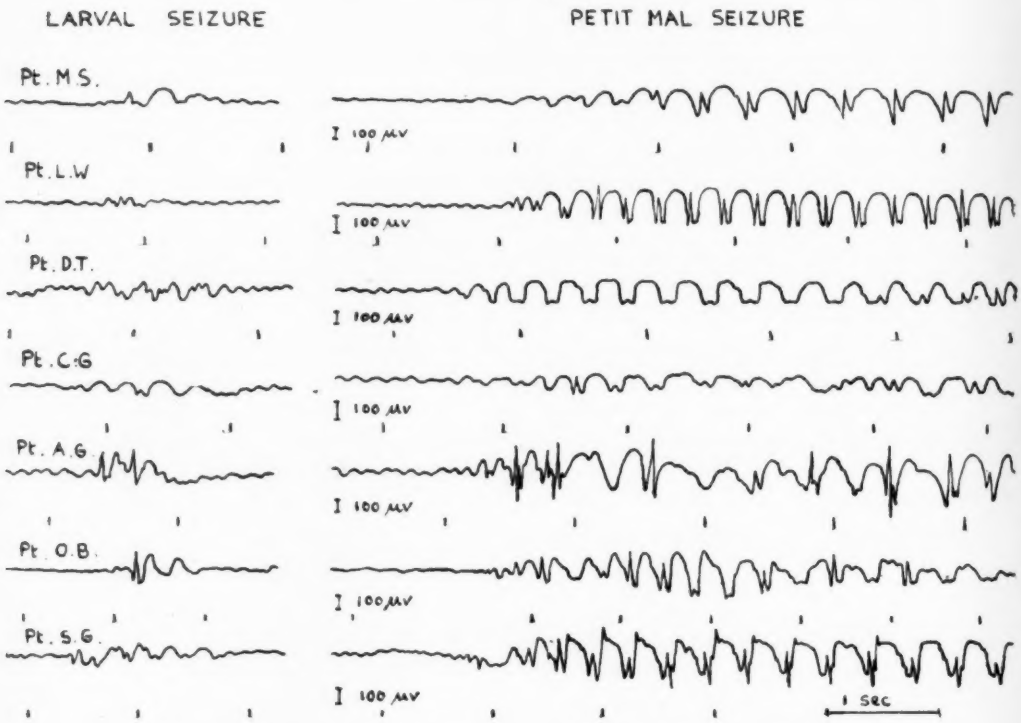

Chart 3.—Alterations of the electro-encephalogram in petit mal epilepsy. Strips were taken from records of different patients. A characteristic wave and spike are obvious in all cases. "Larval seizures" is the term applied to a smaller and shorter electrical disturbance, similar in form to that occurring at the time of a seizure but not associated with loss of consciousness. The height of *I* below each record indicates the deflection of the ink-writing oscillograph produced by a 100 microvolt signal. The vertex becoming electrically negative to the ear gives an upward deflection in all records. The vertical lines below the strips give the time in seconds.

sharp negative spikes in the record often seems to be associated with motor movements of a clonic sort, the rhythm of which is identical with that of the waves, or nearly so. No attempt of the patient to simulate his seizure has ever produced electrical fluctuations like those seen in

a seizure. If the electrodes are securely in place the electro-encephalogram is completely unaltered during such efforts.

GRAND MAL EPILEPSY

In a typical grand mal seizure the electro-encephalogram shows a gradual alteration for fifteen or twenty seconds before any other evidence of the seizure appears. In the nine cases in which we have

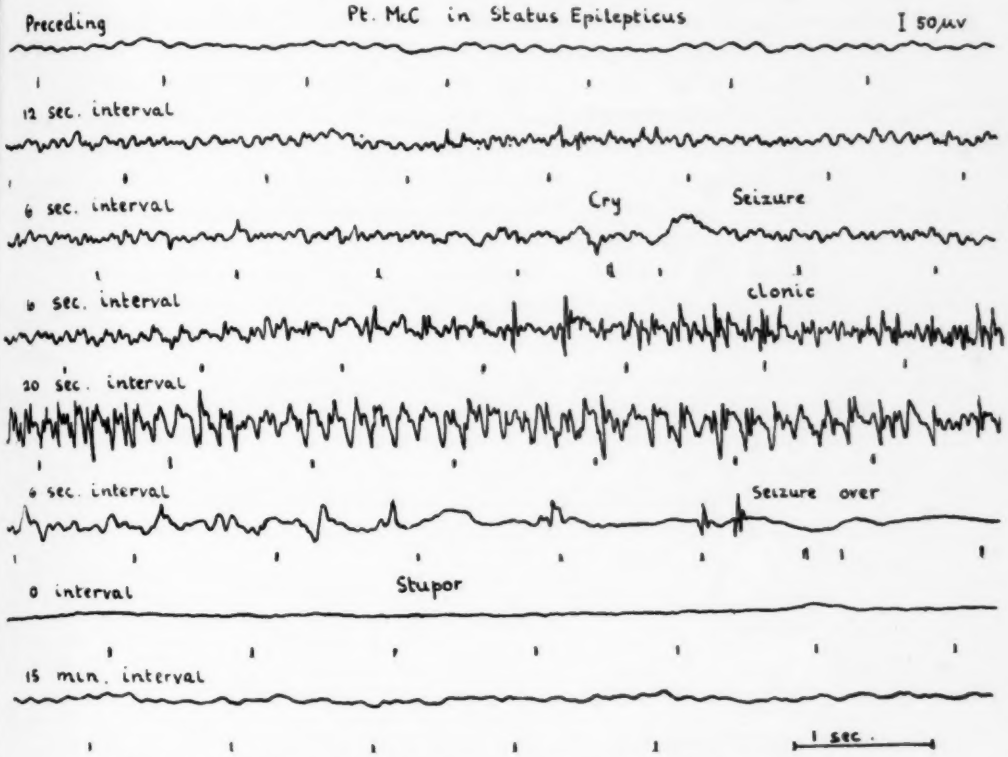

Chart 4.—Alterations in the electro-encephalogram occurring with a grand mal epileptic seizure (patient in status epilepticus). The height of *I* at the end of the first strip indicates the deflection produced by a 50 microvolt signal. The vertex becoming electrically negative to the ear gives an upward deflection. The vertical lines at the bottom of each strip give the time in seconds. Twelve seconds before the clinical onset of the seizure, which was initiated by a cry, the record had markedly altered; this alteration occurred gradually over a fifteen second period. In this patient, as in others with grand mal seizures, the ground electrode in the ear was not used because too many muscle action potentials were obtained (see chart 5); instead, a crown electrode was used as a ground; this eliminated all muscle action potentials except those coming from the highest part of the frontalis muscle, and these did not show with the low amplification needed to record convulsions.

obtained records of grand mal seizures the dominant wave between seizures has had a frequency of from 5 to 18 per second, with the slower frequencies more prominent in the definitely deteriorated patients. This accords with Berger's observations.[12] The first alteration associated with a seizure is that the predominant waves become larger and slightly faster. This occurs before any other evidence that a seizure is about to occur. As the waves continue to increase in amplitude, the cry is given, and the tonic phase of the seizure sets in. As the seizure progresses, slow rhythms appear mixed with the fast ones. Gradually the electrical activity dies down, more or less parallel with the subsidence of muscular activity. Following the seizure the electro-encephalogram is abnormally flat. It remains so for a period which corresponds roughly to the duration of the stupor. It gradually resumes its original characteristics in about twenty minutes (chart 4). Though the seizures may differ greatly from one another in type and amount of muscular movement, the general alterations occurring in the electro-encephalograms all correspond closely to the foregoing description of a typical case.

The sequence of alterations in the electro-encephalogram corresponds to what Fischer [13] has described in animals in which convulsions were induced by drugs. We have corroborated much of Fischer's work on animals and have also noted similar electrical changes when convulsions are produced by electrical stimulation of the brain. Berger has published short records made during grand mal epileptic seizures [14] which show essentially the same characteristics as our own and has noted the flattening of the record during postconvulsive stupor.[12] Foerster and Altenburger,[3] leading directly from the motor cortex during a convulsion, obtained a record which shows 5 per second waves of increased voltage.

ASPHYXIA, SYNCOPE AND OVERVENTILATION

When a normal subject breathes pure nitrogen, the amplitude of the waves in his electro-encephalogram is gradually increased, and then, while still increasing in amplitude, their frequency is slowed. When the subject becomes unconscious or extremely confused, the predominant wave has a frequency of from 2 to 5 per second and a voltage of from 100 to 150 microvolts (chart 5). These changes were noted in twelve subjects who breathed pure nitrogen to the point of unconsciousness. The same sequence of alterations occurs when a subject faints from inadequate blood supply to the brain (chart 6). Syncope was induced in four cases by administering 3 or 4 grains (0.195 or 0.26 Gm.) of

13. Fischer, M. H.: Elektrobiologische Auswirkung von Krampfgiften am zentralen Nervensystem, Med. Klin. **29**:15, 1933.

14. Berger.[1e]

sodium nitrite and then asking the subject to stand quietly for some minutes. Prolonged voluntary overventilation of the lungs with room air in ten subjects also produced an increase in the amplitude of the waves, the frequency of which was from 10 to 20 per second, and then as the subject became confused the frequency slowed to about 5 per second (chart 7).

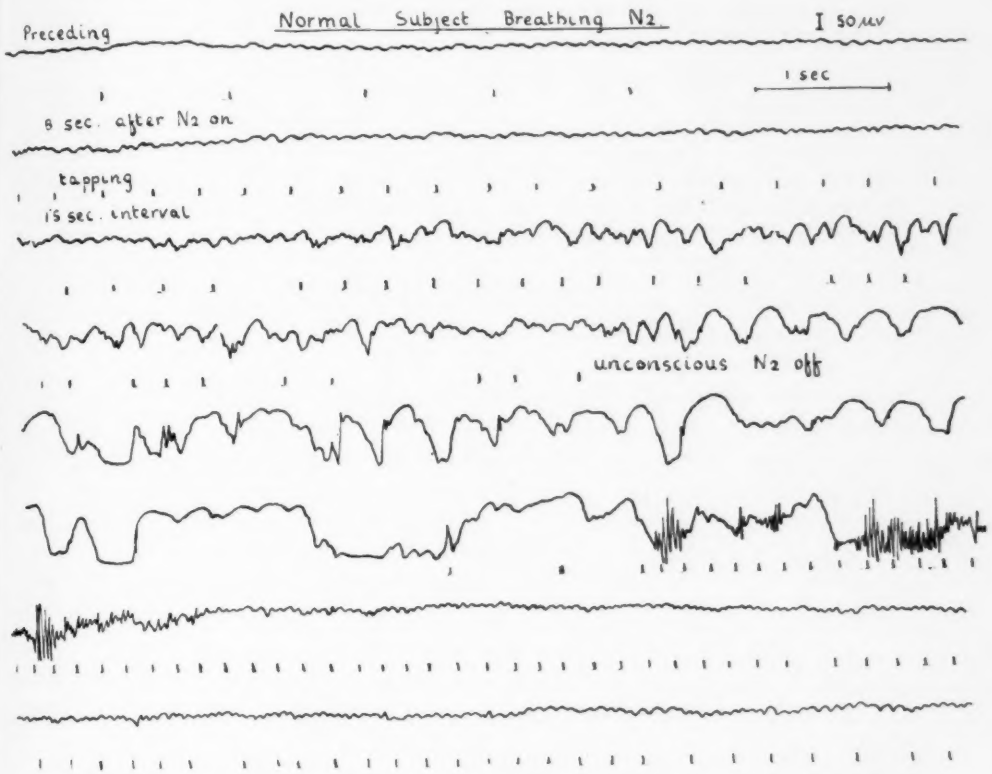

Chart 5.—Alterations in the electro-encephalogram of a normal subject with unconsciousness produced by breathing nitrogen. The height of the *I* at the end of the first strip indicates the deflection produced by a 50 microvolt signal. The vertex becoming electrically negative to the ear gives an upward deflection. The vertical dashes at the bottom of the first strip give time calibration in seconds. Except where indicated, the record is continuous. The vertical dashes on the other strips were made by the subject tapping a signal key. He was instructed to tap continuously and regularly. During the period of unconsciousness he was urged to keep on tapping, so that first taps, as consciousness was regained, were in response to a command. Normal consciousness was not regained until several seconds after tapping was recommenced. The large fast spikes which appeared as consciousness was regained were caused by movements of the jaw. They have the form and frequency of muscle action potentials and probably come from the temporal muscle. They are not properly part of the electro-encephalogram.

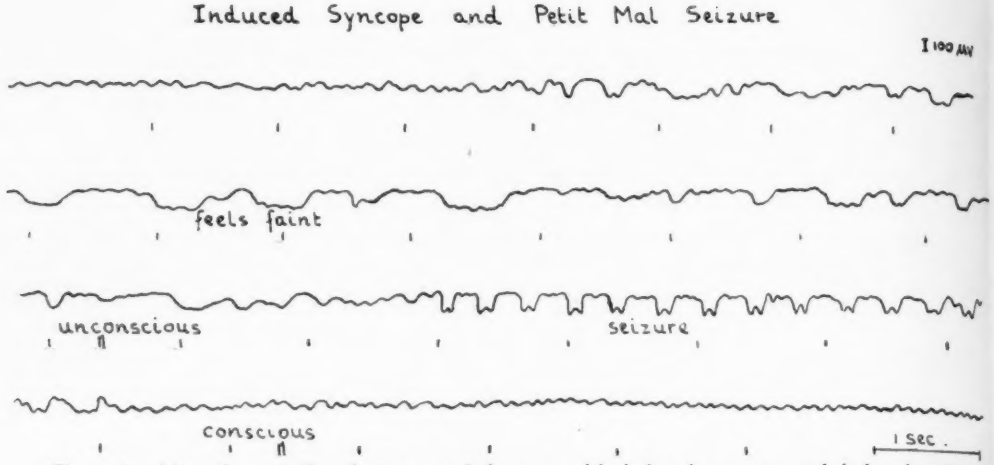

Chart 6.—Alteration of the electro-encephalogram with induced syncope and induced petit mal seizure. Syncope was induced by tipping the patient into the vertical head-up position after he had been given 4 grains of sodium nitrite. As soon as the patient became unconscious, he was tipped back to horizontal. Instead of regaining consciousness at once he had a petit mal seizure. The height of the *I* at the end of the first strip shows the deflection produced by a 100 microvolt signal. The vertex becoming electrically negative to the ear gives an upward deflection. The vertical lines at the bottom of each strip give the time in seconds. There is no interval between the strips.

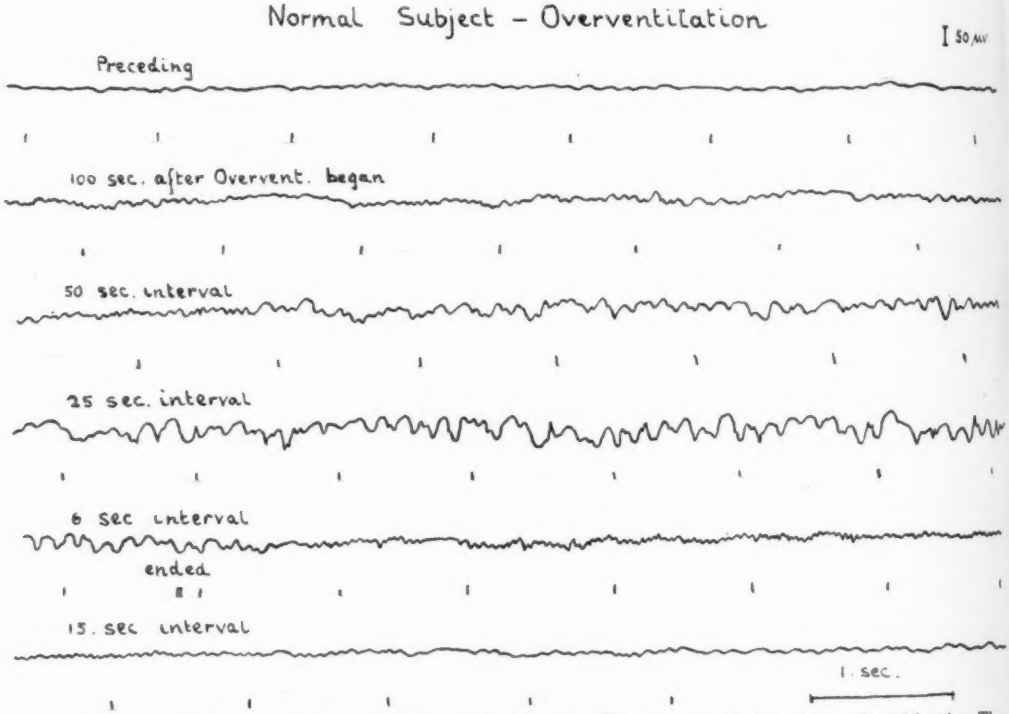

Chart 7.—Alterations of the electro-encephalogram with overventilation (normal subject). The record was made on a normal subject who was instructed to breathe deeply and rapidly in room air. An increase in amplitude and a decrease in the frequency of the waves are discernible as overventilation is continued. The height of the *I* at the end of the first strip indicates the deflection produced by a 50 microvolt signal; the vertex becoming electrically negative to the ear gives an upward deflection. The vertical lines below each strip give the time in seconds.

These three procedures, nitrogen breathing, standing with a lowered blood pressure and overventilation, all of which produced large, slow waves in normal subjects, also tend to precipitate seizures in epileptic persons (chart 6). The differences in wave pattern, notably the characteristic form of the electro-encephalogram in petit mal, made it possible to distinguish clearly between simple loss of consciousness and a seizure. Though it is possible for an epileptic patient to lose consciousness from anoxemia or circulatory failure without a seizure occurring (we have seen this many times), it is nevertheless clear that anoxemia and acute circulatory failure tend to precipitate seizures.

COMMENT

It might seem that we here have evidence that seizures are due solely to cerebral anoxemia. We ourselves are not disposed toward this interpretation because of other evidence indicating that spontaneous seizures are not related to cerebral anoxemia.[15] It is possible to precipitate petit mal seizures by procedures not directed toward a diminution of the cerebral oxygen supply. Two of the patients with grand mal seizures whom we studied could be thrown into seizure by a loud noise. The noise was followed within a tenth of a second by the seizure. Cerebral anoxemia could hardly have occurred in so short a time. It seems more reasonable to suppose that in epilepsy there is a defective central nervous system mechanism which is always ready to show this explosive reaction. The threshold for this reaction can be raised or lowered. Anoxemia is one of the modifications of internal environment which lower it.

Bremer[16] has shown that in what he calls the "isolated" cerebral cortex of the cat electrical activity is reduced by sudden ischemia. He did not mention a preliminary increase in amplitude or a decrease in frequency of the waves. We are presenting here, through the kindness of Drs. H. N. Simpson and A. J. Derbyshire,[17] a record (chart 8) of the effect of ligation of both common carotid arteries on the electrical activity of the cortex of a cat anesthetized with pentobarbital sodium. Before the subsidence of electrical activity, a very slow wave appears which probably corresponds to the slow wave we have seen during syncope and during unconsciousness from breathing nitrogen. It is altogether likely that the final flatness would have supervened in our cases also, as it does with cats, if the oxygen supply had been still

15. Gibbs, F. A.; Lennox, W. G., and Gibbs, E. I.: Cerebral Blood Flow Preceding and Accompanying Epileptic Seizures in Man, Arch. Neurol. & Psychiat. **32**:257 (Aug.) 1934.

16. Bremer, F.: Quelques propriétés de l'activité électrique du cortex cérébral "isolé," Compt. rend. Soc. belge de biol. **118**:1241, 1935.

17. Simpson, H. N., and Derbyshire, A. J.: Electrical Activity of the Motor Cortex During Cerebral Anemia, Am. J. Physiol. **109**:99, 1934.

further diminished or the cerebral circulation more seriously impaired. Bremer [16] reported that asphyxia produces a decrease in the electrical activity of the cortex, leaving only large irregular waves which are not, he believed, of cortical origin. Leaving aside the question of the non-cortical origin of the large waves, it will be seen that Bremer's observation on this point is in general accord with our own. He said, however, that overventilation of the lungs produced in his animals no definite changes in the electrical activity of the cortex.

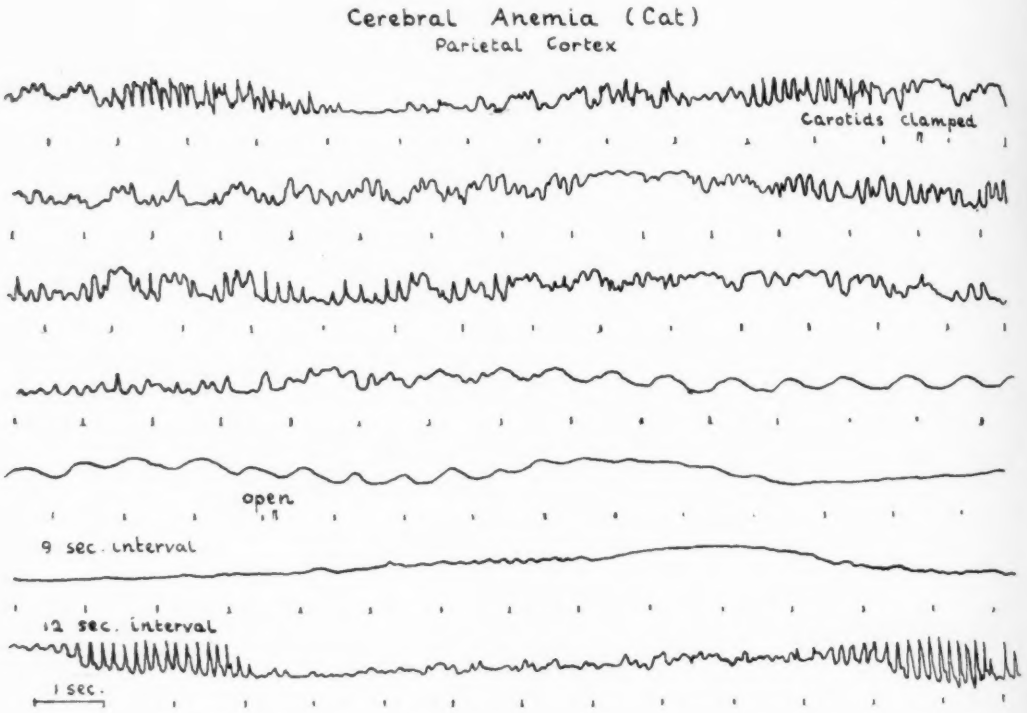

Chart 8.—Effect of ligation of both common carotid arteries on electroencephalogram of a cat (Simpson and Derbyshire). The grid lead used was a wick electrode on the parietal cortex; the ground, a silver plate over the occipital region. The vertical lines under each strip give the time in seconds. The animal was under anesthesia with pentobarbital sodium, which accounts for the variation in electrical activity, for this anesthesia tends to make the cortical waves appear in bursts. Forty seconds after closure of the common carotid arteries, 7 per second waves disappear and are replaced by a slow smooth wave which after eighteen seconds likewise disappears, leaving the record almost flat. In the meantime, the carotid arteries were released; twenty-six seconds after release, the 7 per second waves reappear. Similar changes were observed in this animal in records taken from the motor, the temporal and the occipital cortex. The flattening was greatest for the motor and least for the occipital cortex, probably owing to the distribution of the remaining blood supply from the vertebral arteries.

It is too early to attempt a detailed fundamental interpretation of our data. Available evidence is not sufficient to indicate the real significance of the changes we have observed, but these changes are definite and characteristic. They provide an immediate aid to diagnosis and offer a new avenue of approach to the study of the neural mechanism underlying sudden loss of consciousness. They point the way to an understanding of the neurologic basis of epilepsy.

SUMMARY

The fluctuations in electric potential that originate in the brains of human subjects have been studied with special reference to the manner in which they are altered in epileptic seizures and other conditions characterized by disturbances of consciousness, notably sleep, unconsciousness from breathing nitrogen, unconsciousness from failure of the cerebral blood supply and clouding of consciousness from overventilation.

Standard leads were: a needle thrust into the scalp at the vertex of the head as a grid lead and, except in studies on grand mal seizures, a similar needle in the lobe of the ear as a ground. For studies on grand mal epilepsy, a diffuse electrode in the form of a crown was used. The most constant and pronounced fluctuations observable in the resting subject with these leads have frequencies of from 10 to 20 per second and attain a maximum of 60 microvolts.

In sleep the frequency of these predominant waves decreases to between 1 and 5 per second. Their amplitude also may decrease as the subject falls asleep, if the subject is one who when awake shows waves of large amplitude; but this change is only temporary, for during deep sleep waves of large amplitude and slow frequency appear, often in rhythmic bursts. These may have a voltage of 200 microvolts (chart 2).

In patients suffering from frequent attacks of petit mal epilepsy, groups of large, slow waves appear associated with the seizures. They attain a voltage of from 100 to 300 microvolts at a frequency of 3 per second, showing in all cases a characteristic form (chart 3). They are approximately sinusoidal but usually include a sharp negative spike near the positive crest so that the record at times forms a perfect "egg and dart" design. The spike often appears late in the seizure and tends to disappear before the seizure is over.

Grand mal epileptic seizures are preceded by the gradual appearance of waves having a somewhat higher frequency than those which have been previously dominant. These waves increase in amplitude, and the convulsion begins. The waves continue to increase in amplitude, the frequency remaining about the same. As the clonic phase sets in, the

fast waves tend to clump together into slower waves at about 5 per second. As the convulsive movements die down, the amplitude and also the frequency of the waves decrease, so that during the postconvulsive stupor the record is nearly flat (chart 4).

If a subject becomes unconscious from breathing nitrogen, the frequency of his predominant waves decreases to between 1 and 5 per second, and the amplitude increases to about 200 microvolts (chart 5). This change occurs rather gradually, beginning definitely before the subject loses consciousness. The same change occurs if a subject becomes unconscious from failure of the cerebral blood supply (chart 6). A similar, but less marked, change occurs if a subject overventilates his lungs in room air (chart 7). The frequency drops to about 5 per second, and the amplitude increases to about 100 microvolts.

Those procedures which tend to produce large, slow waves in the normal subject also tend to produce seizures in patients with epilepsy.

RELATION BETWEEN BINET MENTAL AGE AND MOTOR CHRONAXIA

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The present study was undertaken to determine whether measurements of chronaxia might be of value as indicators of the conditions in the brain associated with intellectual or cognitive performances. Specifically, we wished to determine whether there is any relation between various chronaxic measures and the level of intelligence of a subject as measured by the Binet tests.

Our reason for thinking that a relation may exist lies in the body of evidence that the chronaxias of motor nerves depend on the influence of the higher brain centers. It is possible, then, that the conditions in the brain on which the chronaxias depend are also factors in intellectual performances. If this association does exist, an additional point of attack on the question of the constitutional basis of intelligence will become available. The literature relating to the influence of conditions in the brain on the chronaxias of motor nerves is not altogether unequivocal; the evidence, however, that such an influence exists seemed to us sufficiently strong to warrant studying the question of whether there is any relation between the chronaxias of motor nerves and intelligence.

At this point the precise meaning of the term chronaxia should be recalled. Chronaximetric methods represent an attempt to specify the properties of excitability or irritability of a tissue by determining the length of time electric currents of standard type must pass through the tissue before a response is noted. In determining the chronaxia, two steps are necessary: (1) the determination of the minimal strength of current required for stimulating a tissue with a direct current of long duration (this minimal strength of current is called the rheobase) and (2) the determination of the minimal duration of current necessary for stimulating the tissue with a current twice as strong as the rheobase (this duration is the chronaxia). Chronaxia thus is defined as the

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minimal duration of a pulse of direct current required for stimulating a tissue with a current twice as strong as the rheobase.[1]

It should be noted that the chronaxia of a tissue represents the time coordinate of a particular point on a so-called strength-duration curve. The strength-duration curve is the curve showing the minimal strength of current required for stimulating a tissue as a function of the duration of the current. The pulse of current used in determining the chronaxia is thus represented as a point on this curve, a point the coördinates of which are the chronaxia and twice the rheobase. A great deal of the discussion concerning the adequacy of chronaxia as an index of the excitability of a tissue has revolved about the question of whether this strength-duration curve is of an invariable mathematical form.[2] This question is important but is not of concern in the present study, since we are interested only in the question of whether chronaxia, as empirically determined in the same manner in all subjects, is related to variations in mental age. At a later stage, if different levels of chronaxia are found for subjects of different mental ages, it may be of interest to determine the particular parameters of the strength-duration curve the changes of which are responsible for the changes in chronaxia.

An examination of the reports of experiments in the literature indicates that there are three types of chronaxic phenomena which may be dependent on the influence of the higher centers and the association of which with variations in intelligence should therefore be examined: (1) the chronaxias of motor nerves or at the motor points of muscles, (2) the ratio of the chronaxias of the nerves leading to antagonistic muscles, such as the triceps and the biceps muscles and (3) the degree of fluctuation of the chronaxia of a motor nerve. These three types of phenomena may be referred to as chronaxic indexes. The chronaxias of motor nerves which are in connection with the central nervous system and which may therefore be influenced by the higher centers

1. For a discussion of the concept of chronaxia and surveys of the field see (*a*) Lapicque, L.: L'excitabilité en fonction du temps, Paris, Presses Universitaires de France, 1926. (*b*) Bourguignon, G.: La chronaxie chez l'homme, Paris, Masson & Cie, 1923. (*c*) Quincke, H., and Stein, J.: Chronaxie, Ergebn. d. Physiol. **34**:907, 1932. (*d*) Evans, C. L.: Recent Advances in Physiology, ed. 4, London, J. & A. Churchill, Ltd., 1930, p. 280.

2. (*a*) Rushton, A. H.: Lapicque's Canonical Strength Duration Curve, J. Physiol. **74**:424 (April) 1932. (*b*) Lambert, E. F.; Skinner, B. F., and Forbes, A.: Some Conditions Affecting Intensity and Duration Thresholds in Motor Nerve, with Reference to Chronaxie of Subordination, Am. J. Physiol. **106**:721 (Dec.) 1933. (*c*) Sakamoto, S.: Elektrische Reizung einer einzelnen motorischen Nervenfaser durch Gleichspannung, Arch. f. d. ges. Physiol. **231**:489, 1933. Grundfest, H.: Excitability of the Single Fibre Nerve-Muscle Complex, J. Physiol. **76**:95 (Sept.) 1932.

are referred to as chronaxias of subordination; the chronaxias of nerves cut off from their connection with the central nervous system are referred to as chronaxias of constitution.[3] The chronaxias measured at the motor points of muscles in the intact subject may be considered as chronaxias of subordination, for the available evidence indicates that such measurements represent the chronaxias of the motor nerve fibers supplying the muscle rather than those of the muscle tissue itself.[4]

SUBJECTS

The investigation was carried out with fifty male subjects who were distributed equally in the Binet mental age groups of 3, 6, 9, 12 and 15 years. All were more than 17 years old; their intelligence quotients were therefore proportional to their mental ages. The mental and chronological ages of the persons in the various mental age groups are shown in table 1.

TABLE 1.—*Chronological Ages and Mental Ages of the Groups of Subjects*

Mental Age Group, Years	Chronological Age, Years		Mental Age, Years		
	Average	Limits of Range	Examination Number*	Average	Limits of Range
3	26.3	17 to 38	1	2.7	1.2 to 3.8
			2	2.7	1.3 to 3.8
6	23.6	20 to 30	1	6.5	5.7 to 7.2
			2	6.7	6.0 to 7.3
9	26.1	20 to 38	1	9.2	7.8 to 10.5
			2	9.4	8.3 to 9.9
12	29.0	18 to 49	1	11.8	9.6 to 14.1
			2	11.9	11.0 to 13.2
15 (normal)	27.5	20 to 44		15 (assumed)	

* Examination 2 refers to the most recent Binet examinations.

The Binet ratings of mental age, which served as the basis for selection of the subjects, were all made by members of the clinical division of the Vineland Laboratory. The tests used were the Stanford-Binet test for mental ages of 3 years and more and the Kuhlmann-Binet test for mental ages of less than 3 years. The subjects were selected on the basis of the most recent Binet examination that had been given, and an indication of the precision of the measurement was obtained by comparing the results with those of the previous examination. The interval between the two most recent examinations was one-half year or more. The changes in the measurements of the mental age of the individual subjects from the first examination to the second were both positive and negative and in no case greater than 14 per cent.

As shown in table 1, the average mental ages of the different groups varied very little from one examination to the next, and may be regarded as representing a close approximation to the correct average mental ages, assuming the absence of constant errors. Although the averages for the different groups did not fall exactly

3. Lapicque, L., and Lapicque, M.: La chronaxie de subordination; sa régulation réflexe, Compt. rend. Soc. de biol. **99**:1947, 1928.

4. Bourguignon,[1b] p. 16. Bourguignon, G., and Bennati, D.: Les chronaxies motrices et sensitives en pathologie, J. méd. franç. **20**:336 (Sept.) 1931.

at mental ages 3, 6, 9 and 12 years, we shall for convenience refer to the groups in terms of these levels, which are at the midpoints of the intervals taken as a basis for the selection of subjects. For convenience of discussion we shall use the term mentally deficient to refer collectively to subjects in the mental age groups of 12 years and less.[5]

The subjects comprising the group with a mental age of 15 years were selected from among the members of the laboratory and school departments of the Training School at Vineland. It was not considered necessary to give intelligence tests to those subjects, since other criteria, such as the level of former education and occupation, indicated that they could be regarded as having an intelligence at least normal. We have given the mental age of this group as 15 years, as representing the midpoint of the interval from 14 to 16 years, the interval within which the average mental age of normal adults is generally assumed to fall.

Since in the present study we were interested in the dependence of chronaxia on mental age, it was necessary to keep the factors other than mental age which might have influenced the chronaxia substantially constant for the different groups. For that reason the following types of subjects were excluded from the experimental group: subjects with motor disorders (such as spastic or flaccid paralyses, rigidities or athetoid and choreic conditions), epileptic subjects, subjects with mongolism and subjects with glandular disorders, marked emotional excitability, left-handedness or considerable fatty tissue.

Evidence of whether motor disorders, epilepsy or glandular disorders were present was obtained from the medical records available for all persons in the institution. Evidence of the presence or absence of extreme emotional excitability or mongolism was obtained from the regular psychologic reports, which are available for each subject.

Estimates of whether excessive fatty tissue was present were based on our own examination. It was considered desirable to exclude subjects with excessive fatty tissue, since the presence of this tissue tends to introduce errors in the measurement of chronaxia in a number of ways: (1) by increasing the difficulty of observing the response of muscle fibers under the fatty tissue, (2) by increasing the ease with which an electrode placed on the skin may move relative to underlying muscle tissue and (3) by tending to produce abnormally large chronaxias due to the occurrence of an "alpha effect." The term "alpha effect" refers to the abnormally large chronaxias reported as associated with certain distortions of the strength-duration curve. Such distortions have been reported on the use of fluid electrodes with excised preparations and in measurements on human beings with excessive fatty tissue, or when the electrode is displaced from the motor point.[6] By thus eliminating subjects with excessive fatty tissue from our experimental

5. This use of the term is not intended to imply that the sole criterion of mental deficiency is an intellectual one. In the present study, however, we limit ourselves to a consideration of the mental age variable. A discussion of the criteria of mental deficiency is given by E. A. Doll (Criteria of Mental Deficiency, Psychol. Exchange **3**:207, 1935).

6. (*a*) Lapicque, L.: On Electric Stimulation of Muscle Through Ringer's Solution, J. Physiol. **73**:219 (Nov.) 1931; Retrograde Polarization; Theory of Systematic Errors in Measurements of Muscular Chronaxy Through Ringer's Fluid or with Large Electrodes, ibid. **76**:261 (Oct.) 1932. (*b*) Büssow, H.: Ueber Reizzeit-Spannungskurven und Chronaxie am menschlichen Nerv und Muskel, Arch. f. d. ges. Physiol. **231**:689, 1933.

group, we attempted to avoid the possibility that this factor might lead to differences in chronaxic measures for the different groups.

Determination of the handedness of our subjects was made through the use of the inventory compiled by Lauterbach [7] for that purpose. All subjects with a score of less than 50, that is to say, subjects who performed more than 50 per cent of the tasks in the inventory with the left hand, were excluded. These were eliminated from the experimental group in view of the fact that all our measurements were made upon the right arm, and of the evidence reported by Jasper [8] of a tendency for chronaxias at the motor point to be decreased on the preferred side. An inspection of Jasper's data shows that the average chronaxia on the right side of his left-handed subjects was greater than that of his right-handed subjects. An excessive number of left-handed subjects in any one of our groups would thus have tended to increase the average chronaxia of that group.

APPARATUS AND PROCEDURE

Apparatus.—A condenser discharge type of apparatus, similar to that used by Bourguignon [9] (though differing somewhat in detail), was used for making the chronaxic measurements. A diagram of the apparatus is shown in figure 1.

As indicated in the definition of chronaxia already given, the standard form of pulse, on the basis of which the chronaxia of a tissue is specified, is rectilinear, that is to say, a pulse of current which reaches its maximum value instantaneously and which after a certain duration of flow is instantaneously reduced to zero. In practice, however, it is often more convenient to use a stimulating pulse of the form produced by a condenser discharge, as by means of the apparatus pictured in figure 1. The pulse of current produced by this apparatus reaches its maximum intensity at the first instant and then decreases in accordance with an exponential law. When the current has fallen below a certain value, it is no longer effective in exciting the tissue; the duration of the part of the pulse which is effective as a stimulus is proportional to RC, R being the resistance of the discharge circuit and C, the capacity of the condenser. If the resistance of the discharge circuit is kept constant, the properties of the pulse produced may be determined by control of the capacity of the condenser and the voltage to which it is charged. The potential to which the condenser is charged determines the initial strength of current through the subject, and the capacity of the condenser determines the effective duration of the pulse. Accordingly, the chronaxia may be determined in units of capacity (chronaxic capacity) by first determining, as the rheobase, the voltage necessary to stimulate the muscle when the condenser is set at a large capacity and then determining the minimal capacity required for stimulation with a voltage twice the rheobasic voltage.

The chronaxia in units of time may then be calculated by the use of the formula $t = 0.37\ RC$ (t being the time in seconds; R, the resistance of the

7. Lauterbach, C. E.: The Measurement of Handedness, J. Genetic Psychol. **43**:207, 1933.

8. Jasper, H. H.: A Laboratory Study of Diagnostic Indices of Bilateral Neuro-Muscular Organization in Stutterers and Normal Speakers, Psychological Monographs, Princeton, N. J., Psychological Review Company, 1932, vol. 43, pp. 132 and 164.

9. For reports of the investigations on which Bourguignon's technic are based see Bourguignon,[1b] p. 15. The technic used in the present study follows that of Bourguignon in all essentials.

discharge circuit in ohms, and C, the capacity of the condenser in farads). Lapicque[10] reported that he determined the constant 0.37 empirically by comparing the chronaxia of certain tissues as determined in units of capacity with the chronaxia as determined in seconds with the use of rectilinear pulses. With the particular values of resistance used in the circuit in figure 1 and with the resistance of the subject assumed to be equal to 10,000 ohms, the total resistance of the discharge circuit equals 10,666 ohms. The formula thus becomes $t_{ms} = 3.95$ C or, to a close enough approximation, $t_{ms} = 4$ C, if t is measured in milliseconds and C in microfarads.[11]

The apparatus shown in figure 1 is operated as follows: The voltage used for charging the condenser is regulated by means of r_1 and sw_1, r_1 providing for fine adjustments and sw_1 for coarse adjustments. To charge the condenser, sw_2 is left in contact at G, and the key (K) is pressed so as to make contact at B.

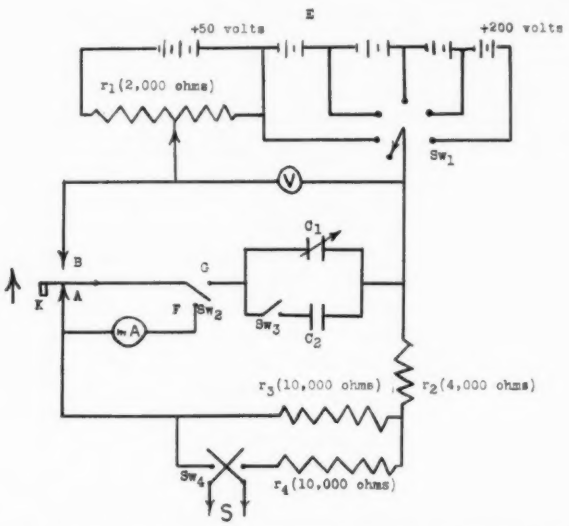

Fig. 1.—Diagram of the circuit of the condenser discharge stimulator. *E* indicates power supply (dry batteries); r_1, variable resistance used as potentiometer; r_2, r_3, r_4, fixed resistances (all resistances are noninductive); C_1, decade condenser (0.001 to 1.11 microfarads); C_2, 10 microfarad condenser; Sw_1, rotary selector switch; Sw_2, Sw_3, knife switches; Sw_4, reversing switch; *K*, tapping key; *V*, high resistance voltmeter (200 volt range, 1,000 ohms per volt); *mA*, milliammeter.

When the key is released, contact is made at A again, and the condenser discharges through the circuit containing the subject. Sw_4 is used for reversing the direction of the current through the subject. To send a continuous current through the subject, sw_2 is closed to make contact at F, and a continuous current flows on key K making contact at B. The strength of the total current may be read on the milliammeter.

In the formula for determining the chronaxia in units of time, it is assumed that the resistance of the discharge circuit remains substantially constant. A

10. Lapicque,[1a] p. 323.

11. Bourguignon,[1b] p. 82.

resistance network like that shown is conventionally used, so that large fluctuations of resistance in the subject will produce relatively small differences in the total resistance. Thus a change of resistance in the subject of from 2,000 to 50,000 ohms would lead to a change in the total resistance of from 9,450 to 12,570 ohms. Despite the provision of this resistance network, it seemed desirable to obtain evidence of the average level of resistance of the discharge circuit for the different groups of subjects, in order to determine whether differences in the level of chronaxia that might be found could be attributed to differences in the level of resistance. Therefore, after each series of chronaximetric determinations on a subject, the conductance of the discharge circuit for continuous currents was determined by setting the applied voltage at 20 volts and measuring the current through the circuit. The resistance could then be readily calculated on the basis of Ohm's law.

The duration of the pulses of current used in these measurements was about one second, the time found necessary for the pointer of the milliammeter to reach a stable position and for the experimenter to obtain a reading. The maximum total current recorded in any measurement was 1.7 milliamperes. The current through the branch to the subject would of course be considerably less, as is indicated by the constants for the discharge circuit given in figure 1. Thus, for a total current of 1.7 milliamperes, simple calculations based on Ohm's law show that the current through the subject would be but 0.34 milliampere.

Electrodes.—Nonpolarizable electrodes of the silver-silver chloride type were used for both active (negative) and indifferent (positive) electrodes. The active electrode consisted of a disk of pure silver, 1.2 cm. in diameter, electrolytically coated with silver chloride and covered with three layers of canton flannel. The indifferent electrode consisted of a flexible piece of pure silver measuring 9 by 11 cm., coated with silver chloride and covered with three layers of canton flannel. In the preparation of each of the electrodes the silver was first covered with the canton flannel, and the layer of silver chloride was then deposited on the silver by passing a current of 15 milliamperes through a 0.4 per cent solution of sodium chloride for one hour, with the electrode serving as the anode and another piece of silver as the cathode. Before being applied to the subject, each of the electrodes was soaked in a 0.4 per cent solution of sodium chloride. The indifferent electrode was applied to the sternum and held in place by two elastic straps passing around the chest. The active electrode was fixed at the end of a metal rod with an insulated handle and applied by hand to the motor point to be stimulated. This electrode was applied, and the muscular response was observed by one of us (G. K.) and the apparatus manipulated by the other (K. B.).

Motor Points Examined.—The motor points examined in this study were those of the biceps brachii, the lateral head of the triceps brachii and the lateral fibers of the brachialis muscle, all of the right arm. These points were selected since they are readily accessible and provide representatives of both flexor and extensor muscles.

The motor point of the biceps muscle may be readily located on the belly of the muscle, as illustrated in the familiar diagrams of the motor points based on those of Erb. The motor point of the lateral head of the triceps is located on the lateral surface of the arm near its junction with the dorsal surface and proximal to the lateral epicondyle by about one fourth of the distance to the acromion process. The location of this point corresponds approximately to that

given by Bourguignon [12] for the posterior point of the lateral head of the triceps muscle.

The motor point of the lateral fibers of the brachialis muscle is located in the lateral bicipital sulcus and proximal to the anticubital fossa by about one third of the distance to the axilla. This point was stimulated by pressing the electrode down into the fissure and against the underlying brachialis muscle. In this particular region of the arm a number of different types of response may be obtained, varying with the exact position of the electrode. The point which we used in this investigation was the one stimulation of which produced a slow movement of the bulge of the muscle just dorsal to the electrode.

The location of this point corresponds to that described by Bourguignon [12] for the anterior point of the lateral head of the triceps.[12] But our observations of the fibers responding on stimulation of this point lead us to regard it as a motor point of the brachialis and not of the triceps muscle. The fibers dorsal to the electrode which respond on stimulation may be readily felt with the fingers as running distad and ventrad along the course known to be taken by the brachialis muscle. We do not regard this point as a desirable one to use in future investigations because of the variation in type of response within a relatively small radius of application of the electrode, and the fact that the electrode, which is pressed down into the fissure in order to stimulate this point, may readily slip about on the underlying tissues.

Procedure Followed in Making Chronaximetric Determinations.—The subject was seated in a swivel office chair on the right side of which was mounted a broad board to support his arm. The forearm was placed in the prone position, making an angle of about 90 degrees with the humerus. The subject could readily be swung about in the chair, so that motor points on the ventral and lateral surfaces of the upper arm were easily accessible.

The sequence of operations performed in making a given determination was as follows:

1. Location of the Motor Point: With the capacity of the stimulator set at 0.3 microfarad, the active electrode was applied to the general region where the motor point is known to be located, and the voltage was increased by large steps until a response was obtained. The active electrode was then moved about in that region, and the voltage was decreased to a level such that a barely perceptible response of the muscle concerned could be observed for just one location of the stimulating electrode. The outline of the contour of the electrode was drawn on the skin with a wax skin pencil, and the region about this outline was again explored by placing the center of the electrode over various points on the circumference of the circle outlined.

Considerable care was thus used in locating the motor point as precisely as possible. After a motor point had been located the site was verified throughout the course of subsequent determinations. Thus, in the determination of the rheobase or the chronaxic capacity, the immediate region adjacent to the marked area was reexplored to determine whether the original area that had been marked still represented the optimal point. If any deviation was noted the motor point was redetermined, and a new determination of the rheobase and the chronaxia was made. In the course of a given determination of the chronaxia the subject was not allowed to move his arm, so that a shift of the apparent motor point would not occur as a result of a change in the position of the arm.

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12. Bourguignon, G.: Double point moteur et double chronaxie du vaste externe du triceps brachial et de l'abducteur du gros orteil de l'homme, Compte rend. Soc. de biol. **110**:520, 1932.

2. Determination of the Rheobase: The condenser was set at 10 microfarads, and the voltage was gradually raised until a just noticeable response of the muscle was obtained. The minimum voltage at which a response could be obtained in two consecutive stimulations was regarded as the rheobase. The smallest step by which the voltage was raised after failure to obtain a response was 2.5 volts.

3. Determination of the Chronaxic Capacity: The voltage was set at a value equal to twice the rheobase; the condenser was set at the capacity expected, on the basis of previous experience, to be less than the chronaxic capacity, and the capacity was raised in successive trials until a just noticeable response of the muscle was obtained. The minimum capacity at which a response was obtained in two consecutive trials was accepted as the chronaxic capacity. The smallest step by which the capacity was increased after failure to obtain a response was 0.005 microfarad. This value also represents the minimum capacity that was used at the beginning of any series.

4. Checking the Rheobase: The procedure outlined for finding the rheobase was then repeated to make certain that the rheobase had not shifted appreciably in the interval required for finding the chronaxia. If it had shifted by more than 2 volts, a new chronaxic value was determined. Shifts of the rheobase were rather infrequent; generally the chronaxic capacity determined in the first trial could be accepted as correct for that determination.

After the chronaxia had been obtained for each of the three motor points investigated in this study, the resistance of the discharge circuit was determined as described in an earlier section. Three separate measures of the chronaxia and of the resistance of the discharge circuit were obtained for each motor point.

To avoid any possibility that an unconscious bias influenced the results, the experimenter observing the response (G. K.) remained unaware of the settings of capacity and voltage used. He merely observed the response and directed the other experimenter (K. B.) to change the voltage or capacity by a given amount. The initial settings in the series were determined by the second experimenter (K. B.). After each trial with the active electrode negative, the reversing switch was adjusted, and a pulse of current was sent through the subject in the opposite direction, in order to minimize the possibility of errors due to polarization. Readings were of course taken only with the active electrode negative.

Calculations of the Chronaxic Indexes.—As indicated in the introduction, three so-called chronaxic indexes were examined: the level of chronaxia, the ratio of the chronaxias at motor points of antagonistic muscles and the range of variation of the chronaxia. To obtain the level of chronaxia of the individual subjects, the average of the three measures made for each motor point of each subject was determined. To represent the ratio of the chronaxias of antagonistic muscles for the individual subjects, the ratio of the chronaxia at the motor point of the triceps muscle to that at the motor point of the biceps muscle was used. The values of the chronaxias used in the calculation were the averages of the three measurements of the chronaxia. The range of variation for each motor point was determined by subtracting the smallest chronaxia recorded from the largest.

RESULTS

A summary of the coefficients of correlation found between the mental age and the various chronaxic indexes is given in table 2. The Pearson coefficients of correlation (r), designed for linear relationships, are given in column 3. As a criterion of reliability, we may

adopt the conventional one that r should be at least four times its probable error. This ratio represents a probability close to 1 that a correlation greater than zero will be found in future samples. On this basis, none of the Pearson r correlations was found to be reliable.

The last three columns of table 2 give the statistics relating to the correlation ratio eta (η). Eta, it will be recalled, is designed as a measure of correlation when the relation between two variables is nonlinear and represents the degree to which the points on the scatter diagram cluster about the line connecting the averages of the various arrays.[13] The etas recorded in the table have been corrected by means of Pearson's[14] formula for errors dependent on the number of arrays and the size of the population. In the case of this index of correlation,

TABLE 2.—*Coefficient of Correlation and Correlation Ratio Between Mental Age and Various Chronaxic Indexes*

Correlation	Muscles	Correlation Coefficient (r)	Probable Error (PE)	$\frac{r}{PE}$	Correlation Ratio* η	Probable Error (PE)	$\frac{\eta}{PE}$
Mental age with level of chronaxia	Biceps	+0.08	0.10	0.8	0.00	0.10	0.0
	Brachialis, lateral part	−0.01	0.10	0.1	0.27	0.09	3.0
	Triceps, lateral head	−0.25	0.09	2.7	0.29	0.09	3.2
Mental age with ratio of chronaxias of antagonist muscles	$\frac{\text{Triceps (lat. head)}}{\text{Biceps}}$	−0.05	0.09	0.5	0.17	0.09	1.8
Mental age with range of variation of chronaxia	Biceps	−0.20	0.09	2.2	0.22	0.09	2.4
	Brachialis, lateral part	−0.13	0.09	1.4	0.22	0.09	2.4
	Triceps, lateral head	−0.23	0.09	2.5	0.33	0.09	3.6

* Corrected.

too, we found no evidence of a reliable correlation, that is to say, of a correlation ratio greater than four times its probable error. Our data, then, fail to exhibit any evidence of a reliable correlation, holding throughout the entire range of mental ages, between any of the chronaxic indexes considered and the mental age.

It is possible, however, even though a reliable correlation does not exist between mental age and a given chronaxic index throughout the entire range of mental ages, that a reliable difference between the averages for some particular group of feebleminded subjects and a group of normal subjects may exist. For this reason, the statistics

13. Rietz, H. L.: Mathematical Statistics, Chicago, Open Court Publishing Company, 1929, p. 90.

14. Pearson, K.: On the Correction Necessary for the Correlation Ratio η, Biometrika **14**:417, 1923.

relating to differences between the averages for the various groups of feebleminded subjects and those for normal subjects were calculated for each of the chronaxic indexes. These statistics are shown in tables 3, 4 and 5. Table 3 shows the dependence of the level of chronaxia on mental age; table 4, the dependence of the chronaxic ratios on mental

TABLE 3.—*Chronaxias and Related Statistics for Various Mental Age Groups in Units of 10^{-5} Second*

Muscle	Statistics*	3 Years	6 Years	9 Years	12 Years	15 Years (Normal)
Biceps	Arithmetical mean.....	7.4	6.8	7.4	7.1	7.2
	σ Dist.	2.0	2.9	2.1	2.6	1.8
	σ M.....	0.36	0.5	0.4	0.5	0.3
	Diff. (FM—N).....	0.2	—0.4	0.2	—0.1	
	σ Diff.	0.5	0.6	0.5	0.6	
	$\frac{D}{\sigma D}$	0.4	0.7	0.4	0.2	
Brachialis, lateral part	Arithmetical mean.....	16.4	11.8	12.0	14.3	14.1
	σ Dist.	6.7	3.2	3.6	5.9	3.4
	σ M.....	1.2	0.6	0.7	1.0	0.6
	Diff. (FM—N).....	2.3	—2.3	—2.1	0.2	
	σ Diff.	1.3	0.8	0.9	1.2	
	$\frac{D}{\sigma D}$	1.7	2.8	2.3	0.1	
Triceps, lateral head	Arithmetical mean.....	10.1	9.9	5.7	8.4	6.5
	σ Dist.	5.8	7.0	2.0	4.9	2.2
	σ M.....	1.06	1.2	0.4	0.9	0.4
	Diff. (FM—N).....	3.6	3.4	—0.8	1.9	
	σ Diff.	1.1	1.3	0.6	1.0	
	$\frac{D}{\sigma D}$	3.2	2.6	1.3	1.9	

* In this and the following tables σ Dist. indicates the standard deviation of the distribution; σM, the standard error of the mean; Diff. (FM-N), the difference of the means of feebleminded and normal groups; σ Diff., the standard error of this difference; and $\frac{D}{\sigma D}$ the ratio of the difference of the means to its standard error.

TABLE 4.—*Ratio of Chronaxia of the Triceps to That of the Biceps Muscle and Related Statistics for Various Mental Age Groups*

Statistics	3 Years	6 Years	9 Years	12 Years	15 Years (Normal)
Arithmetical mean.....	1.5	1.5	1.1	1.4	1.0
σ Dist.....	1.0	1.0	0.6	1.1	0.4
σ M.....	0.31	0.31	0.19	0.34	0.13
Diff. (FM—N).....	0.5	0.5	0.1	0.4	
σ Diff.....	0.34	0.34	0.23	0.36	
$\frac{D}{\sigma D}$	1.5	1.5	0.4	1.1	

age and table 5, the dependence of range of variation of chronaxia on mental age.

The measure of dispersion and reliability used in this analysis of the results is the standard error (σ). To determine whether a difference between the averages for any group of mentally deficient subjects and the averages for normal subjects may be considered reliable, we may adopt the customary criterion that the difference must be greater than

three times its standard error. Such a ratio represents a probability close to 1 that a difference greater than zero and of the same direction will be found in future samples, if the size of the original sample is sufficiently large.

It should be noted that in making use of such a criterion of the reliability of a difference between two averages, the dispersion of each of the groups considered serves as the basis of calculation of the standard error of the difference, and, consequently, each of the factors tending to produce dispersion in the two groups finds representation. In the measurements made of the chronaxia of the subjects in each of our groups, three factors may be regarded as contributing to the dis-

TABLE 5.—*Range of Variation of Chronaxia and Related Statistics for Various Groups in Units of 10^{-5} Second*

Muscle	Statistics	3 Years	6 Years	9 Years	12 Years	15 Years (Normal)
Biceps	Arithmetical mean.....	1.8	2.6	1.6	2.2	1.0
	σ Dist.	2.39	1.35	0.84	2.57	1.05
	σ M.....	0.75	0.43	0.26	0.81	0.33
	Diff. (FM—N).....	0.8	1.6	0.6	1.2	
	σ Diff.	0.82	0.54	0.42	0.87	
	$\frac{D}{\sigma D}$	1.0	2.9	1.4	1.4	
Brachialis, lateral part	Arithmetical mean.....	3.6	3.4	3.8	2.4	3.0
	σ Dist.	2.63	1.35	4.16	1.84	2.93
	σ M.....	0.83	0.43	1.31	0.58	0.92
	Diff. (FM—N).....	0.6	0.4	0.8	—0.6	
	σ Diff.	1.24	1.02	1.00	1.09	
	$\frac{D}{\sigma D}$	0.5	0.4	0.5	0.6	
Triceps, lateral head	Arithmetical mean.....	2.8	3.4	1.0	1.4	1.8
	σ Dist.	3.42	3.13	1.05	1.90	1.76
	σ M.....	1.08	0.99	0.33	0.60	0.55
	Diff. (FM—N).....	1.0	1.6	—0.8	—0.4	
	σ Diff.	1.21	1.13	0.64	0.81	
	$\frac{D}{\sigma D}$	0.8	1.4	1.3	0.5	

persion and therefore as represented in the magnitude of dispersion found: (1) chance errors in the measurements of the individual chronaxias, (2) individual differences among the subjects of the group and (3) variations in the chronaxia which may occur from moment to moment in the individual subjects.

In the calculation of these statistics, thirty measurements of the level of chronaxia were available for each group, but only ten measurements for each of the other indexes considered, since these indexes were based on relations among the three measurements of chronaxia made of each subject. In the calculation of the standard deviation of the distribution,[15] N—1 was used in place of N in cases in which N was equal to ten, N being used in cases in which it was equal to thirty.

15. Fisher, R. A.: Statistical Methods for Research Workers, London, Oliver & Boyd, 1928, p. 46.

An examination of the tables shows that for the group of subjects with the lowest mental age (3 years) at the motor point of the triceps muscle the average level of chronaxia was 0.036 millisecond greater than the normal average and that this difference was more than three times its standard error. Provisionally, it may therefore be regarded as representing a real difference. This difference represents an excess of 55 per cent over the average level for the group of normal subjects. In the case of the other chronaxic indexes and of the other groups of mentally deficient subjects, reliable differences from the normal were not found.

In figure 2 are shown the curves representing the dependence of the level of chronaxia on mental age. The curve for the point of the

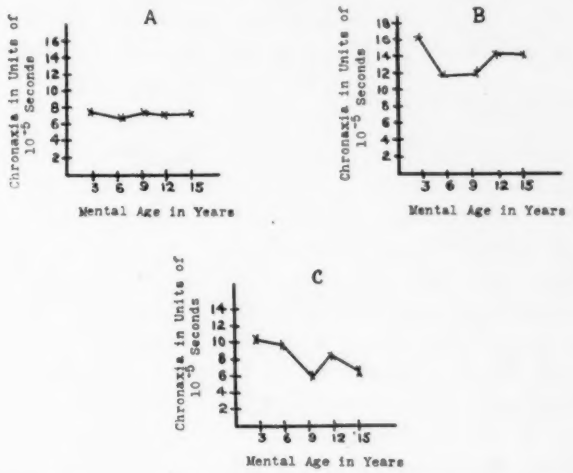

Fig. 2.—Chart showing the level of chronaxia as a function of mental age. *A*, chronaxia of the biceps muscle; *B*, of the lateral part of the brachialis muscle, and *C*, of the lateral head of the triceps muscle, in units of 10^{-5} seconds.

biceps muscle shows a striking constancy of level of chronaxia for all mental ages. The level for the point on the brachialis muscle varies markedly from group to group, but without any definite trend. The differences are, however, unreliable. The curve for the point of the triceps muscle shows a distinct downward trend, indicating an inverse relationship between the level of chronaxia and the mental age. This is reflected in the coefficient of correlation (r), which equals —0.25 (the highest correlation coefficient found for any of the motor points or indexes). However, on the basis of the statistical criteria adopted, we are justified in attaching significance only to the difference between the group of subjects with a mental age of 3 years and the normal

subjects. The curve is of interest, however, in suggesting that groups of mentally deficient subjects of even higher grade may be characterized by higher levels of chronaxia in certain muscles. When it becomes possible in the future to increase the precision of chronaxic measurements, the differences represented in the curve for the other groups of mentally deficient subjects may prove to be indicative of real differences from the normal.

The results of our analysis may be summarized as follows: 1. Evidence was not found of reliable correlations between the mental age and the various chronaxic indexes which hold throughout a range of mental ages extending from 1.3 to 15 years. 2. The average chronaxia of the motor point of the triceps muscle was reliably greater than the normal for the subjects with a mental age of 3 years (by about 55 per cent); but no reliable difference from the normal value was found for groups of subjects of other mental ages, or for the other motor points examined.

COMMENT

What working hypothesis can now be suggested to account for the results obtained and to serve as the basis for further research? There are three features that must be accounted for by any hypothesis: (1) the fact that only the group of subjects of the lowest mental age showed a level of chronaxia reliably different from that of the normal, (2) the fact that this difference in level was found only for the motor point of the triceps muscle (an extensor muscle) but not for those of the brachialis and biceps muscles (flexor muscles) and (3) the fact that the difference consisted of a higher level of chronaxia for the group of subjects of low mental age.

Certain of the factors which might have led to differences in the level of chronaxia in the various mental age groups we attempted to keep constant by excluding subjects with certain characteristics from the experimental group and by the precautions taken to apply a fixed procedure in the measurement of all subjects. The factors which we attempted to control have been indicated in previous sections.

Among the factors which remain for further consideration are: the level of electrical resistance in the two groups, differences in the stability of the motor point (the "shifting phenomenon") and differences in the stage of development of the nervous system.

1. *Possible Influence of Differences in Resistance on the Level of Chronaxia.*—The determinations of chronaxia made in the present study were based on the assumption that the resistance of the discharge circuit was substantially constant for all groups of subjects and that the varia tions in duration of the pulse were determined only by variations in the capacity. If, however, a difference in the average level of resistance

for the subjects of low mental age and for normal subjects existed, it would tend to introduce corresponding differences in the chronaxic measures.

The measurements of conductance made on each subject and described in the section on apparatus make it possible to determine the approximate level of resistance of the discharge circuit when the subject is included in the circuit. Table 6 shows the average level of resistance of the discharge circuit for each group of subjects, the difference between the normal group and each of the groups of mentally deficient subjects, and the ratio of this difference to the normal level expressed in percentage. As the table shows, the percentage of difference between the various groups of mentally deficient subjects and the group of normal subjects is nowhere greater than 5 per cent and so

TABLE 6.—*Level of Resistance of Discharge Circuit for Various Mental Age Groups*

Active Electrode Applied at Motor Point	Statistics	Average Level of Resistance in Ohms and Related Statistics				
		3 Years	6 Years	9 Years	12 Years	15 Years (Normal)
Biceps	Arithmetical mean	12,420	12,350	12,050	11,910	12,000
	σ Dist.	617	305	290	426	286
	Diff. (FM—N)	420	350	50	—10	0
	Diff. / Normal average	4%	3%	0%	0%	
Brachialis, lateral part	Arithmetical mean	12,200	11,830	11,630	11,630	11,630
	σ Dist.	602	350	473	270	203
	Diff. (FM—N)	570	200	0	0	0
	Diff. / Normal average	5%	2%	0%	0%	
Triceps, lateral head	Arithmetical mean	12,120	11,830	11,770	11,490	11,760
	σ Dist.	735	210	415	264	208
	Diff. (FM—N)	360	70	10	—270	0
	Diff. / Normal average	3%	1%	0%	—2%	

may be disregarded as an appreciable factor in the results. Of particular interest are the relative levels of the subjects with a mental age of 3 years and the normal subjects when the electrode was applied to the motor point of the triceps muscle. The average level of resistance for the group of subjects with a mental age of 3 years was 3 per cent greater than that for the group of normal subjects. This difference is statistically unreliable ($\sigma_D = 140$ ohms; $D/\sigma_D = 2.5$) and negligible in amount. Moreover, its direction is such that if a correction were made in the chronaximetric calculations to allow for it, we should obtain a level of chronaxia for the group of subjects with a mental age of 3 years still greater than that found (since the effective duration of the pulse of stimulation is proportional to the resistance multiplied by the capacity). The difference in the level of resistance may accordingly be dismissed as a factor in the higher level of chronaxia found for this group.

2. *Possible Influence of the Difference in the Stability of the Motor Point on the Level of Chronaxia.*—Büssow [6b] and Laugier [16] have pointed out that displacement of the electrode from the motor point may result in positive errors in the measurement of chronaxia; that is, it may result in measurements that are too high. To guard against this source of error, the procedures already mentioned for careful location of the motor point and the use of the same procedure with all subjects was followed. Therefore, in the absence of specific factors associated with any particular group of subjects, there is no reason to believe that the differences in the levels of chronaxia obtained were due to differences in the precision with which the motor point was located.

However, in the course of our measurement of the chronaxias in the different groups, a striking phenomenon was observed in subjects of our lowest mental age group which must be considered as a possible factor in the higher level of chronaxia found. In this group a rather marked instability in the location of the motor points was observed. The best motor point found at one time would often be appreciably displaced from the best point found later in the period. Before a measure of chronaxia was accepted as correct, we made certain that we were still working on the optimal point for obtaining a response. Nevertheless, it is conceivable that displacements of the electrode from the optimal point occurred as a result of the shifting of the motor point and that these shifts played a rôle in the higher levels of chronaxia found for the subjects with a mental age of 3 years.

There is some evidence, however, that the difference in the level of chronaxia found for the triceps muscle cannot be plausibly attributed to a difference in stability of the motor point in the two groups of subjects. In terms of our qualitative observations, the shifting phenomenon was as marked for the other motor points as for the point on the triceps muscle; yet for these other points no reliable difference in the level of chronaxia was found.

This shifting phenomenon, however, merits further investigation in order to determine its possible influence on the measurements of chronaxia and possibly to throw light on physiologic differences between the subjects of low mental age and normal subjects.

3. *Differences in the Stage of Development of the Nervous System.*—Finally, we may consider the possibility that the higher level of chronaxia found in the group of subjects of lowest mental age may have been due to developmental defects of the nervous system. Associated most directly with the large differences in mental age that existed

16. Laugier, H., and Neoussikine, B.: Mesures d'excitabilité, au point moteur et en plein muscle, sur le biceps brachial de l'homme, Compt. rend. Soc. de biol. **111**:940, 1933.

between those subjects and normal subjects, we think most immediately of deficiencies of development, particularly those of the central nervous system. It is necessary to inquire whether our results can be explained on the basis of factors of that type.

We find two lines of evidence in support of that view: (1) the reports that in the course of development the direction of change of the chronaxias of motor nerves and at motor points of muscles is from high to low values and (2) the evidence that the elimination of various levels of the central nervous system leads to an increase in the chronaxias of motor nerves and at motor points of muscles. There is some evidence, too, that the influence of the higher nervous levels is a differential one, affecting to a different extent the chronaxias of the nerves to extensor and flexor muscles. Such a phenomenon makes understandable the fact that we found an increased chronaxia for the motor point of the triceps muscle, but no reliable difference for the motor points of the brachialis and biceps muscles.

1. Reports on Developmental Changes in Chronaxia: Evidence that changes in chronaxia occur during the course of development has been reported by Bourguignon and Banu and by Marinesco, Sager and Kreindler. Bourguignon [17] has reported that in new-born infants the chronaxias at the motor points of muscles are always higher than the values for normal adults, ranging from one and one-half to ten times the normal values. Marinesco [18] has reported that measurements made just after birth on two premature (7 month) infants showed chronaxic values which were still higher than those found in full term infants at birth. Bourguignon and Banu [19] investigated the changes occurring during the course of development and found that normal chronaxic values are reached about 20 months after birth, although in some muscles earlier than in others.

In addition to the data on the development of chronaxia in human beings, investigations have been made on animal fetuses and new-born animals, and the results were in accord with those obtained in human beings. Thus, Banu [20] reported chronaxias at the motor points of animal fetuses and new-born animals that were from ten to fifteen times the values exhibited by adult animals. Marinesco, Sager and

17. Bourguignon,[1b] p. 225.

18. According to a report by Quincke and Stein.[1c] We were unable to locate the original report by Marinesco.

19. Bourguignon,[1b] p. 226. Banu, G., and Bourguignon, G.: Evolution de la chronaxie des nerfs et muscles du membre supérieur des nouveau-nés, Compt. rend. Soc. de biol. **85**:349, 1921.

20. Banu, G.: Recherches physiologiques sur le développement neuromusculaire chez l'homme et l'animal, Thèse sc., Paris, 1922; cited by Quincke and Stein.[1c] Banu's own report in his thesis was not accessible.

Kreindler [21] reported chronaxias for the pyramidal tracts of new-born cats and guinea-pigs about ten times the values found in adult animals. In animals, normal chronaxic values are reached much earlier than in human beings.

It is of interest to consider the relative course of development reported by Bourguignon [22] for the chronaxia at the motor points of the lateral head of the triceps and the biceps muscles, the muscles examined in the present study. In the curves given to represent the course of development, we find that at 2 months the chronaxia of the triceps was eight times the value taken as normal; at 16 months it had reached a value one and one-half times the normal, a deviation from the normal comparable to that of the average found for our subjects with a mental age of 3 years; by 20 months the normal value had been reached. At birth the motor point of the biceps muscle had a chronaxia equal to that of the triceps muscle at 2 months. It decreased rapidly with an increase in age, so that at all stages it was less than the chronaxia of the triceps muscle. At 16 months, when the triceps muscle had a value one and one-half times its normal value, the chronaxia of the biceps muscle had already reached its final normal value.

Our finding of an increased average level of chronaxia for the point of the triceps muscle in the subjects of low mental age with no significant difference for the biceps muscle thus fits in well with the data on development. On the basis of the data just reported, we might regard our subjects of mental age of 3 years, in terms of the average level of the development of chronaxia reached, as comparable with normal infants of about 16 months.

2. Reports on the Influence of Higher Centers on the Level of Chronaxia in Nerves: Lapicque [23] observed in the frog a marked increase (between 60 and 100 per cent) in the chronaxia of the sciatic nerve (observation of the gastrocnemius muscle) on section of the nerve or of the central nervous system beneath the level of the optic lobes. After removal of the cerebral hemispheres alone no appreciable change was observed. Denisoff [24] reported confirmation of Lapicque's results on repetition of the latter's experiments. He also reported that in a certain percentage of his animals little or no change in chronaxia was observed on elimination of the nerve centers.

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21. Marinesco, G.; Sager, O., and Kreindler, A.: Vergleichende Studien über die Chronaxien des Fasc. pyramidalis bei neugeborenen Katzen und Meerschweinchen, Deutsche Ztschr. f. Nervenh. **130**:176, 1933.

22. Bourguignon,[1b] p. 227.

23. Lapicque, M.: Action des centres encéphaliques sur la chronaxie des nerfs moteurs, Compt. rend. Soc. de biol. **88**:46, 1923.

24. Denisoff, P.: Quelques expériences confirmant l'existence de la chronaxie de subordination, Compt. rend. Soc. de biol. **113**:150, 1933.

The Chauchards [25] reported that in the crab there is an increase (about 130 per cent) of the chronaxia of the motor nerve to the flexor muscle of a locomotor appendage on elimination of the cerebral ganglion and a second increase, not quite so marked, on elimination of the subesophageal ganglion. Jasper [26] reported, also for the crab, an increase in the chronaxia of a motor nerve on section of the nerve. He stated that his distribution curves for the level of chronaxia in intact animals suggests the participation of different neural levels in the regulation of chronaxia, as was reported by the Chauchards.

In the cat Marinesco, Sager and Kreindler [27] compared the norms for chronaxias at different motor points with the values obtained after elimination of various parts of the nervous system. Following extirpation of the entire cerebral cortex they found a marked increase (from 100 to 300 per cent) in the chronaxia at the motor points of all of the muscles examined (flexor and extensor digitorum, gastrocnemius and tibialis anticus on both sides of the body). This evidence indicates that in cats, as in crustaceans, according to the Chauchards' report, even the highest neural levels exercise an influence on the chronaxias of peripheral nerves. In frogs, on the contrary, Lapicque's evidence indicated a lack of influence of the cerebral hemispheres.

On the opposite side, however, Lambert, Skinner and Forbes [2b] reported that they were not able to find appreciable changes in the chronaxias of motor nerves after elimination of higher centers except in cases in which section of the nerve was made close to the electrodes. In those cases they attributed the change to a lowered rheobase produced as a result of the current of injury. As they pointed out, their experiments were all carried out on decerebrate animals and so could not indicate the influence of levels above that at which decerebration was performed.

Except for the paper of Marinesco, Sager and Kreindler, none of the studies cited provided any indications that the elimination of a given center is likely to produce different effects on the nerves leading to antagonistic muscles. The data of Marinesco, Sager and Kreindler indicated a much greater rise in chronaxia for the gastrocnemius muscle and the flexor muscles of the toes than for the tibialis and the extensors of the toes. Additional evidence of such differences in effect may be found in the studies made on changes in the ratios of chronaxia

25. Chauchard, A. B., and Chauchard, P.: Influence des centres sur l'excitabilité des nerfs moteurs chez les crustaces, Compt. rend. Soc. de biol. **111**:621, 1932.

26. Jasper, H. H.: L'action des centres nerveux sur la fonction du temps dans l'excitabilité des nerfs moteurs du crabe, Compt. rend. Soc. de biol. **112**:230, 1933.

27. Marinesco, G.; Sager, O., and Kreindler, A.: Die Chronaxien des neuromuskulären Komplexes nach Ausschaltung verschiedener Teile des Zentralnervensystems in chronischen Tierversuchen, Deutsche Ztschr. f. Nervenh. **130**:171, 1933.

of nerves to antagonistic muscles as a result of the elimination of different nerve centers. Studies of these ratios have been made by the Lapicques;[28] Bonvallet and Rudeanu;[29] Jasper and Bonvallet,[30] and Marinesco, Sager, and Kreindler.[27] In many of them further instances of different relative changes in nerves to extensor and flexor muscles may be found. Thus in one of the papers by the Lapicques,[28a] there is an example of changes somewhat analogous to our own findings. After section of the medulla of the frog an increase of 150 per cent was noted in the chronaxia of the nerve fibers to the gastrocnemius muscle, but an increase of only 15 per cent in the chronaxia of the nerve fibers to the tibialis muscle. Such instances may be regarded, however, only as presenting analogies to our results. No data appear in the literature on the changes in chronaxia of the particular muscles which we investigated and in types of animals closer to man, such as anthropoid apes or other primates. To facilitate interpretation of the findings in human subjects, investigations on certain of the primates would seem highly desirable.

A final group of studies are of interest here, since their results may be plausibly accounted for in terms of the influence of the higher centers on the chronaxias of peripheral nerves. Thus, Lapicque [23] reported that after the administration of anesthetics to the frog, the nerve to the gastrocnemius muscle showed a rise equivalent to that occurring after section below the optic lobes. Lambert, Skinner and Forbes,[31] however, reported failure to confirm that result in experiments on one cat and two frogs. Jasper [32] reported differences in the level of the chronaxia on the two sides of the body depending on the handedness or sidedness of the subject. One possible explanation of these results is in terms of the doctrine of cerebral dominance. Monnier and Jasper,[33] in a series of studies, reported that after section of the

28. Lapicque, L., and Lapicque, M.: (*a*) Modifications des chronaxies motrices périphériques par les centres nerveux supérieurs, Compt. rend. Soc. de biol. **99:** 1390, 1928; (*b*) footnote 3.

29. Bonvallet, M., and Rudeanu, A.: Sur le rôle de l'écorce cérébrale dans la régulation des chronaxies motrices, Compt. rend. Soc. de biol. **110:**696, 1932.

30. Jasper, H. H., and Bonvallet, M.: La subordination chez le rat spinal, Compt. rend. Soc. de biol. **113:**1186, 1933.

31. Lambert, Skinner and Forbes,[2b] p. 729.

32. Jasper, H. H.: A Laboratory Study of Diagnostic Indices of Bilateral Neuro-Muscular Organization in Stutterers and Normal Speakers, Psychological Monographs, Princeton, N. J., Psychological Review Company, 1932, vol. 43, pp. 132, 164 and 167.

33. Monnier, A. M., and Jasper, H. H.: Relation entre la vitesse de propagation de l'influx nerveux et la chronaxie de subordination, Compt. rend. Soc. de biol. **110:**286, 1932; Recherche de la relation entre les potentiels d'action élémentaire et la chronaxie de subordination, ibid. **110:**547, 1932; Relation entre le potentiel de démarcation d'un nerf et la chronaxie de subordination: analogie avec l'électrotonus, ibid. **110:**549, 1932.

nerve correlated changes occur in the chronaxia of the motor nerve to the gastrocnemius muscle and in other properties of the nerve, such as magnitude and velocity of propagation of action potential, and in demarcation potential of the nerve. Bourguignon and Haldane [34] reported that with the onset of sleep the chronaxia at the superior motor point of the common extensor muscle of the fingers rises to values 50 per cent greater than normal. Bourguignon and Haldane attributed that change to one in the functional state of the nerve centers during sleep.

Comment.—As this brief review shows, the evidence may be found in the literature to support the hypothesis that the higher level of chronaxia found at the point of the triceps muscle for our group of subjects with a mental age of 3 years may have been due to defects in development of higher nerve centers. This hypothesis is to be regarded as purely provisional, for the facts on which it rests are in no sense conclusively established. Our own result, showing a higher average level of chronaxia for the group of subjects of lowest mental age requires confirmation in view of the relatively small number of cases available and the fact that the statistical criteria used acquire greater significance as the size of the sample increases. Moreover, the evidence cited of the influence of the various central levels on the chronaxias of motor nerves is not sufficiently extensive, and reports on certain questions are conflicting. One of the cardinal defects noted in much of the literature on chronaxia is the failure of the authors to provide any index of the reliability of the results, as by the use of standard statistical devices. This failing makes it difficult to determine the particular directions in which further confirmatory investigation is most needed.

The working hypothesis suggested by our results can be summarized as follows: In adult idiots the brain mechanism which in normal subjects serves to reduce the chronaxia of certain of the motor nerves is in a relatively early stage of development, being comparable to a state of development found in the new-born infant. The locus of these developmental defects is probably in the cortex but possibly may extend to lower levels. Concerning the part these defects play in reducing the mental age of the subjects, either of two alternatives is conceivable: (1) The deficiencies in the brain responsible for the deviations in the chronaxia (if localized in the cortex) may also be factors responsible for the lower mental age, or (2) the deficiencies responsible for the deviations in the chronaxia may not play any part in the deviations in mental age. The tendency for the level of mental

34. Bourguignon, G., and Haldane, J. B. S.: Evolution de la chronaxie pendant le sommeil, Compt. rend. Soc. de biol. **107**:1365, 1931.

age to be associated with the level of chronaxia which we have found may then be accounted for in terms of a parallel course of development of the two systems, such as to result in subjects of low mental age in a lag in the development of the system regulating the chronaxia, as well as in the system underlying intellectual performances.

The hypothesis previously stated, together with other phases of the discussion, indicates a number of subjects on which further research is desirable. Those of most immediate interest are: (1) a more extensive investigation, with a larger number of subjects, to determine whether our finding of a difference between the levels of chronaxia of the subjects with a mental age of 3 years and the normal can be confirmed; (2) extension of the investigation to other groups of muscles in order to determine whether our finding of a difference for extensor but not for flexor muscles holds for other body segments (thus, it should be desirable to investigate reciprocal groups, such as the hamstring and the quadriceps and the tibialis anticus and the gastrocnemius muscle); (3) investigation of the chronaxias at motor points in young subjects with low intelligence quotients (if our hypothesis of a retarded development of the mechanism regulating the chronaxia of idiots is correct, we should expect to find a still lower stage of development, and consequently a still higher level of chronaxia of certain muscles in younger children of idiot grade); (4) investigation of the "shifting phenomenon," (*a*) to determine whether our report of a greater instability of the motor point in subjects of a mental age of 3 years can be confirmed by quantitative studies of the stability of localization of the motor point in the different groups (our own observations were purely qualitative), (*b*) to determine whether this shifting phenomenon is adequate to account for the higher level of chronaxia found in the subjects with a low mental age and (*c*) to determine the physiologic significance of the shifting phenomenon (if the difference reported between mentally deficient and normal subjects can be confirmed, an analysis of its conditions may point to interesting physiologic differences between the two groups).

SUMMARY

The present study was undertaken in the hope of making available additional indirect physiologic methods for investigating the properties of the brain associated with intellectual performances. Reports in the literature have suggested that chronaximetric methods might be of value in that connection. We therefore attempted to answer the question of whether there is a relation between various chronaxic indexes and intelligence as measured in the terms of Binet mental ages.

The indexes examined were the level of chronaxia at the motor points of certain muscles (biceps, brachialis, lateral head of triceps),

the ratio of chronaxias of motor points of antagonistic muscles and the range of fluctuation of chronaxias for individual subjects. We failed to find any reliable correlations between any of these indexes and the mental age which hold for the range of mental ages from 1.3 to 15 years, the range represented by our subjects.

A reliable difference, however, was found between the average level of chronaxia of subjects with a mental age of 3 years and normal subjects for the motor point on the triceps muscle, but not for other motor points, other chronaxic indexes or other mental ages.

A number of possible explanations for these results were considered. The working hypothesis that seems most plausible at the present time is that the higher level of chronaxia found for the subjects in the lowest mental age group is due to developmental defects in the brain. These particular developmental defects may or may not be factors in intellectual performance.

Further tests of this hypothesis remain as problems for future research. An answer to the question of whether chronaximetric methods may prove useful in analyzing the brain conditions associated with mental deficiency must await the completion of investigation along the lines suggested.

CLASSIFICATION OF SCHOOL CHILDREN BY MEANS OF THE HANDWRITING SPEED FACTOR

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Having found experimentally that two hundred unselected adult persons wrote a model test sentence in from twenty-seven to sixty seconds, with an average value of 48.6 seconds, the idea suggested itself that it might be possible to trace out step by step the early stages in the evolution of this time factor if determinations of speed were made among groups of school children. For such tests suitable material was available in the Roman Catholic Orphanage of San Francisco, an institution for girls, in which they are given courses of instruction in the same consecutive grades as in the public school. Without selecting them in any way, one hundred of the students were tested. The age range was from 8 to 17 years.

TECHNIC

The girls were admitted to the examining room one at a time. The specimens of handwriting were obtained in the following manner: On a blank library filing card (76 by 128 mm.) each pupil was asked to write this sentence: "He protested that he couldn't eat the twenty-two tarts; and the truth is that he ate twenty." The time consumed in writing this sentence was determined, without the reactor's knowledge, by means of a stop watch. On completion of each specimen, notations were made on the card of the girl's name, age, grade in school and speed record in seconds.

RESULTS

Relation Between Speed and Age.—The time values recorded for each age group are shown in table 1. On referring to these findings it will be observed at once that (1) the speed values diminish progressively at each successive age level and (2) not only were the figures shown for the ages from 8 to 12 years inclusive much larger than those set down for the ages from 13 to 17 but the figures for the earlier period exhibited a much greater difference between the lowest and the highest value.

If the time data displayed in table 1 are examined again, it will be seen that they were exceptionally large throughout the four year period from the ages of 8 to 11 but that thereafter the values fell away less rapidly. The period mentioned is, however, precisely the one during which a child is supposed to learn how to write—a process the accomplishment of which implies the coordination of a variety of central nervous activities both sensory and motor. The speed data seemed to

show that for some girls this was an easy task while for other girls it was a comparatively difficult one. This supposition seemed to receive support from some other observations. For on comparison at each age level of the two writings that had the smallest and the largest time value, respectively, it was uniformly noted that the specimen produced in the smallest time interval was far superior to the other in neatness, appearance, regularity of alinement and evenness in the spacing of the words.

Relation Between Speed and Grade.—It will be observed (table 1) with reference to the records of grades, particularly those of the first five age groups, that they tended to fall roughly into an order inversely

TABLE 1.—*Classification of One Hundred Orphan Girls in Age Groups with the Records of Their Grade and Handwriting Speed*

Age	Grade	Speed, Sec.	Age	Grade	Speed, Sec.	Age	Grade	Speed, Sec.	Age	Grade	Speed, Sec.
8	3	167	11	7	57	12	5	91	14	1*	57
8	3	252	11	7	62	12	5	107	14	7	72
8	3	255	11	4	73	12	5	131	14	5	79
8	2	288	11	7	76	12	6	136	14	8	81
8	3	305	11	7	88				14	8	86
			11	7	85	13	1*	40	14	7	130
9	4	114	11	4	104	13	8	52			
9	4	129	11	5	110	13	7	54	15	2*	46
9	4	138	11	6	110	13	8	54	15	2*	46
9	5	142	11	5	110	13	7	55	15	2*	51
9	4	142	11	4	120	13	5	56	15	1*	57
9	4	170	11	3	134	13	7	56	15	1*	61
9	2	177	11	5	138	13	7	57	15	8	63
9	3	195	11	4	149	13	7	58	15	1*	64
9	4	207	11	3	169	13	1*	59	15	8	68
9	3	270				13	5	59			
						13	7	62	16	3*	38
10	6	58	12	8	51	13	7	70	16	1*	46
10	5	105	12	6	61	13	7	76	16	1*	49
10	5	106	12	1*	65	13	8	76	16	2*	50
10	4	120	12	8	67				16	1*	60
10	4	121	12	6	71	14	2*	39	16	2*	62
10	4	139	12	3	74	14	5	52	16	7	62
10	4	145	12	8	74	14	1*	55	16	2*	86
10	4	162	12	8	76	14	1*	56			
10	3	180	12	5	85	14	1*	56	17	3*	46
10	3	211	12	6	87	14	8	57	17	1*	46
									17	3*	47

* In high school.

proportional to that of the time values; indeed in one group, that of the girls 10 years of age, it will be noted that the grades formed a fairly regular sequence. This seeming relationship between the speed values and the grade values, it was assumed, was probably not an accidental one owing to faulty data. But to remove any doubt that might exist on this point, the original notes were carefully checked against the records on file at the orphanage. This examination showed (1) that in each instance the record of grades was correct and (2) that in each of the ten age groups studied the student who had written the test sentence in the smallest space of time usually had the best, or nearly the best, scholastic record. Conversely, bradygraphia seemed to be characteristic of a number of the girls who were referred to by the head of the school as being "backward" in their studies.

Mean Values for Age and Speed at Each Grade Level.—These data are displayed in table 2. In brief, they seem to show (1) that during a girl's passage through the various school grades of this orphanage, improvement in her handwriting speed factor took place by steplike degrees and (2) that as measured by means of a model sentence, this speed factor reached the average adult level of 48.6 seconds between the ages of 13 and 17 years among girls enrolled in any one of the first three grades in the high school.

TABLE 2.—*Classification of One Hundred Orphan Girls by Grades to Show for Each Grade the Inclusive Range in Years, the Average Age and the Average Value for Handwriting Speed.**

Grades		Age Data		Average Speed, Sec.
		Range in Years	Average Age	
Grammar School	2	8– 9	8.5	232
	3	8–12	9.4	201
	4	9–11	9.8	137
	5	9–14	11.7	91
	6	10–12	11.5	87
	7	11–16	12.6	70
	8	12–15	13.2	67
High School	1	12–17	14.5	55
	2	14–16	15.2	54
	3	16–17	16.6	43

* For the purpose of comparison, the average adult speed value was estimated to be 48.6 seconds.

SUMMARY

The results obtained in timed experiments in writing made with one hundred orphan girls from 8 to 17 years of age are described.

The mean speed values noted for the ten grades from the second year of grammar school to the third year of high school diminished by steplike degrees from 232 seconds to 43 seconds.

The mean value for adults, 48.6 seconds, was reached only by the high school pupils, and as a rule by girls from 15 to 17 years of age.

On tabulation of the speed values for each age level—in the order from the smallest to the largest—it was noted that the grade values tended to form an inverse sequence; this circumstance suggested the existence of a correlation between the factors of handwriting speed and intelligence.

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CEREBROSPINAL FLUID IN CASES OF TUMORS OF THE BRAIN

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There are numerous reports in the literature on the findings in the cerebrospinal fluid in cases of tumor of the brain. Most of these reports, however, are confined to an analysis of the cell count or the protein content of the fluid in a few cases, and there are few data in the literature on the complete findings at lumbar puncture in a large series of cases. I have thought it advisable, therefore, to report the findings at lumbar puncture in 182 cases in which the diagnosis was confirmed at operation or at necropsy. In addition, I shall present data on the relationship of the protein content of the ventricular fluid and that of the lumbar fluid and on the localizing significance of this relationship in cases of tumor of the brain.

DANGERS OF LUMBAR PUNCTURE IN CASES OF TUMOR OF THE BRAIN

The paucity of reports on the findings in the cerebrospinal fluid in cases of tumor of the brain is due in part to the belief shared by most neurosurgeons that lumbar puncture is contraindicated when such a diagnosis is considered. This belief is probably justified in regard to cases in which there is high grade choked disk or in which the diagnosis is obvious. On the other hand, in many cases the patient is seen in a general hospital and the diagnosis of an expanding lesion cannot be established or excluded without the aid of the data elicited by lumbar puncture or by some operative procedure. This subject was recently discussed by Fremont-Smith and Putnam.[1] They reviewed the reports of fatalities after lumbar puncture and concluded that in a majority of the cases the ordinary precautions had been grossly neglected, and they suggested that in the specialized clinics the possibility of obtaining more information by this method should not be overlooked. They emphasized that most of the fatalities described by Schönbeck [2] occurred

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1. Fremont-Smith, F., and Putnam, T. J.: The Value of Lumbar Puncture in the Diagnosis of Suspected Tumor of the Brain, Arch. Neurol. & Psychiat. **28**:1212 (Nov.) 1932.

2. Schönbeck, O.: Die Gefahren der Lumbalpunktion, Arch. f. klin. Chir. **62**:309, 1915.

in the early days of the use of lumbar puncture and that in the literature since that time many large series have been reported in which such disastrous results did not occur. Masson [3] stated that in only 1 of 200 cases of tumor of the brain in which lumbar puncture had been done could death possibly be attributed to the lumbar puncture. Puusepp [4] also reported that in a large number of cases, including 18 instances of tumor of the posterior fossa, there were no fatalities. Schaller [5] minimized the danger of lumbar puncture in cases of tumor of the brain. In the 182 cases in my series no deaths were attributable to lumbar puncture. It is my belief that lumbar puncture is definitely contraindicated in cases in which there is a high grade choked disk or in which the diagnosis is obvious, but that in cases in which the diagnosis is questionable the information obtained by a carefully performed lumbar puncture will aid in establishing the diagnosis earlier and possibly will permit removal of the tumor before it has reached a prohibitive size. It may also exclude the diagnosis of tumor of the brain and obviate operative procedure in a large number of cases. This is especially true in cases of syphilitic meningitis or cerebral vascular accidents.

METHOD

The method of performing the lumbar puncture is important in the prevention of serious accidents. The puncture should be made only while the patient is in the lateral recumbent position. The danger of making the puncture on a patient with a tumor of the brain while in the sitting position cannot be overemphasized. Most fatalities have occurred when the patient was in this position. The sitting position is especially to be deprecated since the cerebrospinal fluid pressure cannot be measured and its measurement is perhaps the most valuable information to be obtained from the puncture. After careful determination of the pressure, enough fluid should be removed to perform the necessary tests. After the puncture the patient should be kept flat in bed for from twenty-four to forty-eight hours with the foot of the bed elevated.

In the cases reported in this paper the cells were counted in an ordinary blood count chamber, the cells being faintly stained with Unna's polychrome methylene blue. The protein content was determined by the Ayer, Dailey and Fremont-Smith [6] modification of the method of Denis and Ayer; the sugar content, by

3. Masson, C. B.: The Dangers of Diagnostic Lumbar Puncture in Increased Intracranial Pressure Due to Brain Tumor, in Elsberg, C. A., et al.: The Intracranial Pressure in Health and Disease, Baltimore, Williams & Wilkins Company, 1929, p. 422.

4. Puusepp, L.: Die Kleinhirn-Brückenwinkel-Tumoren, Folia neuro-chir. **9**:51, 1929.

5. Schaller, W. F.: Propriety of Diagnostic Lumbar Puncture in Intracranial Hypertension, J. Neurol. & Psychopath. **14**:116, 1933.

6. Ayer, J. B.; Daily, M. E., and Fremont-Smith, F.: Denis-Ayer Method for the Quantitative Estimation of Protein in the Cerebrospinal Fluid, Arch. Neurol. & Psychiat. **26**:1038 (Nov.) 1931.

the method of Folin and Wu as modified by Rothberg and Evans;[7] the chloride content, by the Wilson and Ball[8] modification of the Van Slyke method, and the colloidal gold curve, by the method of Lange as described by Cockrill.[9]

FINDINGS IN THE CEREBROSPINAL FLUID FROM THE LUMBAR REGION

Pressure.—The cerebrospinal fluid pressure in the lumbar region was measured in 168 cases with the patient in the lateral recumbent position by the Ayer or the Fremont-Smith modification of the Ayer water manometer. Readings of pressures of less than 150 mm. are considered normal; those between 150 and 200 mm., high normal or possibly abnormal and those of more than 200 mm., definitely abnormal. The pressure at the first puncture varied from 70 to 700 mm. of cerebrospinal fluid. As shown in table 1, in 148 (89 per cent) of the cases the pressure was more than 150 mm.; in 118 cases (70 per cent), more than

TABLE 1.—*Distribution of One Hundred and Sixty-Eight Cases of Tumor of the Brain on the Basis of the Lumbar Cerebrospinal Fluid Pressure at the First Puncture* *

Location and Type of Tumor	Cerebrospinal Fluid Pressure, Mm. of Cerebrospinal Fluid				Total No. of Cases
	Less Than 150	150–200	200–300	300–700	
Supratentorial					
Glioma	8	9	28	31	76
Meningioma	2	2	4	6	14
Tumor of pituitary fossa	1	4	0	0	5
Other types	4	7	9	7	27
Subtentorial					
Neuroma of acoustic nerve	1	0	5	7	13
Glioma of cerebellum	1	5	4	14	24
Glioma of brain stem	2	3	0	1	6
Other types	1	0	2	0	3
Total number of tumors	20	30	52	66	168

* The puncture was made with the patient in the lateral recumbent position.

200 mm., and in 66 cases (40 per cent), more than 300 mm. Normal or high normal cerebrospinal fluid pressures were common in cases of tumor of the brain stem or the pituitary fossa. In 17 of the 66 cases of glioma of the hemisphere the pressure was less than 200 mm.; in 7 of the 17 cases subsequent punctures were done, and in 5 instances the pressure was more than 200 mm. In five of the remaining 10 cases the tumor showed cystic degeneration. In six of the 24 cases of glioma of the cerebellum the pressure was normal at high normal levels; in 2 of these instances partial subarachnoid block was shown by simultaneous lumbar and ventricular punctures; in a third case intravenous injections of magnesium sulphate had been given a short time before the lumbar puncture. In the 27 cases noted in table 1 as instances of "other supratentorial tumors" the following distribution occurred: varied nongliomatous tumor, 11 cases; meta-

7. Rothberg, V. S., and Evans, F. A.: Modified Folin and Wu Blood Sugar Determination, J. Biol. Chem. **58**:443, 1923.

8. Wilson, D. W., and Ball, F.: Study of Estimation of Chloride in Blood and Serum, J. Biol. Chem. **79**:221, 1928.

9. Cockrill, J. R.: Comparison of Gold Chloride, Benzoin and Mastic Tests on Cerebrospinal Fluid, Arch. Neurol. & Psychiat. **14**:455 (Oct.) 1925.

static carcinoma, 13, and tuberculoma, 3. In 5 of the 11 cases of nongliomatous tumors of the hemisphere the pressure was normal or at a high normal level. Three of these tumors were angiomas, and 1 was a lipoma of the dura. In 5 of the 13 cases of metastatic tumor of the brain the pressure at the first puncture was normal or high normal. In 2 of these 5 cases the pressure was more than 250 mm. at subsequent punctures.

There are few data in the literature in regard to the lumbar cerebrospinal fluid pressure in cases of tumor of the brain. Ayer [10] recorded the findings in 67 cases. His findings are in agreement with mine. He reported a pressure of more than 200 mm. in 18 of 23 cases (78 per cent of subtentorial tumor and in 31 of 40 cases (77 per cent) of supratentorial tumor.

Examination of the fundus oculi does not always give a reliable index of intracranial pressure. The intracranial pressure as measured by lumbar puncture was definitely elevated in a number of my cases in which the optic disks were normal. This was also observed by Ayer.[10] Bollack and Hartmann [11] have reviewed the literature on this subject.

On the other hand, choked disk was occasionally found on examination of the fundus oculi when the lumbar cerebrospinal fluid pressure was normal. In such cases the presumption is that the intracranial pressure was formerly, or is only intermittently, elevated. I found the latter to be true in several cases in my series.

Character of the Fluid.—The fluid was usually clear and colorless, but in 52 cases (28 per cent) it was yellow or xanthochromic. Xanthochromia was present in 4 of 7 cases of tumor of the corpus callosum, in 3 of the 4 cases of glioma of the third ventricle, in 7 of the 16 cases of neuroma of the acoustic nerve and in 27 of the 71 cases of glioma of the hemisphere. This histologic diagnosis in the remaining 11 cases was: metastatic carcinoma in 3 cases, meningioma in 2, glioma of the cerebellum in 1, glioma of the brain stem in 1 and hemangioma of the choroid plexus in 4.

Xanthochromia was associated with a protein content of more than 100 mg. per hundred cubic centimeters in all but 7 cases. In 4 of the 7 cases a few hundred or a few thousand red cells were present in the fluid, and the xanthochromia could be explained as due to hemolysis of blood extravasated from the tumor.

The frequency of occurrence of xanthochromic cerebrospinal fluid in cases of tumor of the brain was found by Comfort [12] to be 20 per cent of 75 cases; by Ayer,[10] 19 per cent of 67, and by Greenfield and Carmichael,[13] 13 per cent of 54. Dunlap [14] found xanthochromic lumbar fluid in 6 of 22 cases of metastatic tumor of the brain. Ironside and Guttmacher [15] observed xanthochromia in the fluid in 4 of 7 cases of tumor of the corpus callosum.

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10. Ayer, J. B.: Cerebrospinal Fluid in Brain Tumor: Analysis of Sixty-Seven Cases of Tumors and Cysts of the Brain, J. A. M. A. **90**:1521 (May 12) 1928.

11. Bollack, J., and Hartmann, E.: Diagnostic et traitement des tumeurs cérébrales, Rev. neurol. **1**:949, 1928.

12. Comfort, M. W.: Yellow Spinal Fluid Associated with Tumor of the Brain, Arch. Neurol. & Psychiat. **15**:751 (June) 1926.

13. Greenfield, J. G., and Carmichael, E. A.: The Cerebrospinal Fluid in Clinical Diagnosis, New York, The Macmillan Company, 1925.

14. Dunlap, H. F.: Metastatic Malignant Tumors of the Brain, Ann. Int. Med. **5**:1274, 1932.

15. Ironside, R., and Guttmacher, M.: The Corpus Callosum and Its Tumours, Brain **52**:442, 1929.

Cells.—The cell count was recorded at the first puncture in 165 cases. The results varied from 0 to 4,000 white cells per cubic millimeter. In 21 per cent of the cases there were no cells in the fluid; in 71 per cent, less than 6, and in 83 per cent, less than 10. In 4 cases (3 per cent) there were more than 100 cells, and in 1 case, an instance of glioma of the corpus callosum, more than 1,000 white cells, per cubic millimeter. In 6 cases in which there were no or less than 6 white cells at the first puncture, pleocytosis with a white cell count of 8, 22, 42, 44, 132 and 320 cells, per cubic millimeter, respectively, was noted at subsequent punctures. In 1 case of glioma of the corpus callosum in which there were 8 cells per cubic millimeter at the first puncture, coma supervened three days later. The lumbar fluid then showed 4,000 white cells. The findings in the cerebrospinal fluid in this case and in the other case in which there were more than 1,000 cells per cubic millimeter have been previously reported [16] and are shown in table 2. In the 35 cases in which there were more than 10 white cells per cubic millimeter in the cerebrospinal fluid at the first lumbar puncture or at subsequent punctures, the following distribution occurred: 16 cases of glioma of the hemisphere, with 12, 12, 14, 15, 16, 17, 22, 41, 42, 67, 78, 100, 132, 141, 174

TABLE 2.—*Findings in the Cerebrospinal Fluid in Two Cases of Glioma of the Corpus Callosum with Marked Pleocytosis in the Lumbar Cerebrospinal Fluid*

Case	Date	Pressure, Mm. of Cerebrospinal Fluid	White Cells, No. per Cu.Mm.	Protein, Mg. per 100 Cc.	Sugar, Mg. per 100 Cc.	Sodium Chloride, Mg. per 100 Cc.	Colloidal Gold Curve
1	2/ 7/29	450	2,106	216	80	696	0001110000
	2/ 8/29	300	3,000	426	75	705	0011110000
2	10/26/31	...	8	82	74	...	0012300000
	10/29/31	250	4,000	235	43	...	0000121000
	11/ 1/31	170	80	160	66	...	.....

and 320 cells, respectively; 5 cases of glioma of the cerebellum, with 12, 14, 25, 80 and 135 cells, respectively; 5 cases of glioma of the corpus callosum, with 44, 45, 198, 3,000 and 4,000 cells, respectively; 4 cases of metastatic carcinoma, with 13, 22, 30 and 73 cells, respectively; 2 cases of hemangioma of the choroid plexus, with 92 and 119 cells, respectively; 1 case of adenoma of the pituitary gland, with 50 cells; 1 of meningioma, with 11 cells, and 1 of tuberculoma with 12 cells.

The occurrence of slight or moderate pleocytosis in the lumbar cerebrospinal fluid in cases of a tumor of the brain was noted by Greenfield and Carmichael [13] in 11 of 54 cases, by Moersch [17] in 20 of 127 cases, by Ayer [10] in 12 of 58 cases and by Smith [18] in 26 of 102 cases. Marked pleocytosis in the lumbar cerebrospinal fluid had been noted by Parker [19] in a case of glioma of the temporal lobe,

16. Merritt, H. H., and Moore, M.: Tumours of the Brain Associated with a Marked Pleocytosis in the Cerebrospinal Fluid, J. Neurol. & Psychopath. **13**: 118, 1932.

17. Moersch, F. P.: Serology in Brain Tumor, J. Nerv. & Ment. Dis. **58**:16, 1923.

18. Smith, J. C.: Tumor cerebri, Pleocytosis spinalis und die Eiweissverhältnisse der Spinalflüssigkeit, Deutsches Ztschr. f. Nervenh. **89**:278, 1926.

19. Parker, H. L.: Tumour of the Brain Associated with Diffuse Softening and Turbid Cerebrospinal Fluid, J. Neurol. & Psychopath. **10**:1, 1929.

with a count of 1,707 cells in the fluid; by Moersch [17] in a case of glioma of the corpus callosum, with 679 cells; by Merwath [20] in 2 cases of glioma of the corpus callosum and in 1 of tumor in the interpeduncular region, with 2,015, 2,000 and 600 cells, respectively, and by Christiansen [21] in 2 cases of tumor in the region of the optic chiasm, with 20,000 and 500 cells, respectively.

The white cells in the cerebrospinal fluid were usually lymphocytes or mononuclear cells, except in 2 cases in which the cell count was very high and polymorphonuclear leukocytes constituted over 90 per cent of the total count. Occasionally, tumor cells may be found in the fluid, especially in cases of medulloblastoma.

The pleocytosis in the lumbar cerebrospinal fluid in cases of tumor of the cerebellum or cerebrum is due to an aseptic meningeal reaction produced by necrosis of brain or tumor tissue near the ventricle. In the 2 cases of marked pleocytosis in the lumbar fluid in this series, necropsy showed a glioma of the corpus callosum and both frontal lobes with a large fresh hemorrhage and

TABLE 3.—*Distribution in One Hundred and Eighty-Two Cases of Tumor of the Brain on the Basis of the Protein Content of the Lumbar Cerebrospinal Fluid*

Location and Type of Tumor	Protein Content of Lumbar Cerebrospinal Fluid, Mg. per 100 Cc.					Total No. of Each Type
	Less Than 45	45–100	100–200	200–500	500–1,500	
Supratentorial						
Glioma	23	32	15	9	2	81
Meningioma	4	7	4	0	0	15
Tumor of the pituitary fossa	2	3	0	0	0	5
Other types	10	13	5	2	0	30
Subtentorial						
Neuroma of acoustic nerve	0	2	3	11	0	16
Glioma of cerebellum	12	7	3	1	0	23
Glioma of brain stem	3	2	0	1	0	6
Other types	2	1	2	1	0	6
Total number of cases	56	67	32	25	2	182

necrosis of the tumor and the ventricular walls. The case recorded by Moersch [17] and 2 of the cases reported by Merwath [20] were also instances of gliomas of the corpus callosum and adjacent portions of the frontal lobes. In the case of Parker a glioma of the temporal lobe had caused occlusion of the middle cerebral artery and necrosis of the area supplied by it. In the cases reported by Christiansen [21] and in 1 described by Merwath [20] the tumor was in the region of the optic chiasm. Christiansen explained the pleocytosis in these cases as due to localized meningitis resulting from erosion of the nasal sinuses by the tumor.

Protein Content.—The protein content of the fluid was determined in 182 cases. The results varied from 15 to 1,920 mg. per hundred cubic centimeters. Table 3 shows that in 126 cases (70 per cent) the fluid had a protein content higher than 45 mg., the upper limit for normal values in my series. In 59 cases (32 per cent) the protein content was higher than 100 mg. In 2 cases—one of glioma of the third ventricle in which the protein content was 684 mg. and one of glioma of

20. Merwath, H. R.: Unusually High Cellular Reaction in Cerebrospinal Fluids in Brain Tumors, M. Times & Long Island M. J. **61**:227, 1933.

21. Christiansen, V.: Les tumeurs dans la région du chiasma avec pléocytose concomitante, Rev. neurol. **2**:113, 1924.

the temporal lobe in which the content was 1,920 mg.—the protein content of the fluids was more than 500 mg.

In cases of tumor above the tentorium high values for the protein content of the lumbar fluid were constant when the tumor was a glioma of the third ventricle or of the corpus callosum. In cases of tumor of the cerebral hemisphere there were normal values for the protein content, unless the ventricular walls were involved.

In the group of subtentorial tumors an increased protein content was constant in cases of neuroma of the acoustic nerve. In approximately 50 per cent of the cases of tumor of the cerebellum or fourth ventricle there was a normal amount of protein in the lumbar fluid. The level of the protein content of the lumbar fluid was often of value in the differential diagnosis of tumors of the cerebellum and neuroma of the acoustic nerve since in cases of the latter the protein content was usually between 150 and 500 mg. while in those of the former the values usually ranged from 20 to 150 mg.

An increased protein content of the lumbar cerebrospinal fluid has been noted in from 40 to 75 per cent of cases by all the authors who have written on this subject. Smith [18] obtained a positive reaction to the globulin test in 43 of 96 cases, and Moersch,[17] in 67 of 127 cases. Ayer [10] reported increased protein content in 73 per cent of 67 cases, and Greenfield and Carmichael,[13] in 44 per cent of 54 cases.

Colloidal Gold Reaction.—The colloidal gold test was performed in 159 cases. In 60 cases (37 per cent) a normal reaction was obtained; in 50 others (32 per cent) no greater change than the appearance of lilac ("2") was shown; in 38 (24 per cent) a midzone curve (0123321000) was obtained; in 6 (4 per cent), a first zone curve (5554321000), and in 5 (3 per cent), an end-zone curve (0001122333). The following pathologic diagnoses were made in the 6 cases in which a first zone curve was obtained: glioma of the hemisphere, glioma of the cerebellum, glioma of the brain stem and metastatic carcinoma in 1 case each and neuroma of the acoustic nerve in 2 cases. The Wassermann reactions of the blood and cerebrospinal fluid were negative in all 6 cases.

Abnormal colloidal gold curves have been noted by Ayer [10] and Moersch.[17]

Sugar Content.—The sugar content of the lumbar fluid was determined in 115 cases. The results varied from 41 to 164 mg., with an average of 75 mg., per hundred cubic centimeters. In only 4 cases was there less than 50 mg., and in only 8, more than 100 mg.

Chloride Content.—The chloride content of the fluid was determined in 101 cases. The results, expressed in milligrams of sodium chloride, varied from 597 to 847 mg., with an average of 720 mg., per hundred cubic centimeters. In the majority of the cases there was a chloride content of from 700 to 750 mg. In a few cases values between 650 and 700 mg. were obtained. These low values were probably due to a decrease in the chloride content of the blood associated with vomiting. In 2 cases the chloride content was higher than 800 mg. as the result of a recent intravenous injection of hypertonic saline solution. In 2 cases of glioma of the third ventricle the chloride values ranged from 597 to 623 mg. Such a marked reduction in the chloride content has not been observed in any other cases. It is possible that tumors in this region may have a special effect on the metabolism of chlorides.

Wassermann Reaction.—The Wassermann reactions of the blood and cerebrospinal fluid were both strongly positive in 2 cases. In 2 other cases the Wassermann reaction of the cerebrospinal fluid was positive and that of the blood

negative. In none of these 4 cases was gross evidence of syphilis of the nervous system presented at necropsy. Two similar cases were recorded by Nonne,[22] and the literature offers numerous isolated examples.

THE VENTRICULAR FLUID

Puncture of the lateral ventricles through trephine openings in the skull gives information as to the size and location of the ventricles, thus aiding in the localization of intracranial neoplasms. In addition, a comparison of the protein content of the fluid from the two lateral ventricles with that of the lumbar fluid gives definite aid in determining the site of the tumor. Fremont-Smith and Hodgson [23] have shown that if simultaneous lumbar and ventricular punctures are performed the comparison of the response to compression of the jugular vein of the pressure recorded by the lumbar manometer with that recorded by the ventricular manometer is frequently of aid in differentiating subtentorial and supratentorial tumors. Partial or complete dynamic block is often found in cases of subtentorial tumor.

The fluid from the lateral ventricles is normal unless the ventricular walls are involved by the tumor; then the fluid from the ventricles may be xanthochromic and show increased protein content and an abnormal colloidal gold reaction.

I have found pleocytosis in the ventricular fluid in only 5 cases. In an instance of metastatic carcinoma there were 960 cells in the fluid of the right ventricle and 360 in that of the left. In 4 cases of glioma of the hemisphere 10, 10, 16 and 80 cells, respectively, were present in the fluid from the homolateral ventricle.

PROTEIN CONTENT OF THE VENTRICULAR FLUID

The protein content of the ventricular fluid is the most significant finding. This has been previously emphasized by Fremont-Smith.[24] A comparison of the protein content of the ventricular fluid with that of the lumbar fluid is presented here. The cases have been divided into two groups according to the protein content of the fluid from the lumbar region.

1. *Cases in Which the Protein Content of the Lumbar Fluid Was Normal.*—I have analyzed the protein content of fluid from the lateral ventricles in 30 cases in which the protein content of the lumbar fluid was normal. In all these

22. Nonne, M.: Syphilis und Nervensystem, ed. 4, Berlin, S. Karger, 1921, p. 141.

23. Fremont-Smith, F., and Hodgson, J. S.: Combined Ventricular and Lumbar Puncture in the Diagnosis of Brain Tumor, in Dana, C. L., et al.: The Human Cerebrospinal Fluid, New York, Paul B. Hoeber, Inc., 1926, p. 172.

24. Fremont-Smith, F.: Cerebrospinal Fluid in Differential Diagnosis of Brain Tumor, Arch. Neurol. & Psychiat. **27**:691 (March) 1932.

cases except 1 the fluid from the lateral ventricles had a normal protein content. This case was an instance of glioma of the hemisphere. The fluid from the homolateral ventricle was xanthochromic and had a protein content of 3,400 mg. per hundred cubic centimeters. Air injected into this ventricle did not pass into the opposite or the third ventricle, and at operation the foramen of Monro was observed to be occluded by the tumor.

TABLE 4.—*Comparison of the Protein Content of the Lumbar Fluid and That of the Ventricular Fluid in Twenty-Six Cases of Tumor in the Posterior Fossa in Which the Protein Content of the Lumbar Fluid Is Increased*

	Protein Content, Mg. per 100 Cc.				Protein Content, Mg. per 100 Cc.			
		Ventricular Fluid				Ventricular Fluid		
Type of Tumor	Lumbar Fluid	Right	Left	Type of Tumor	Lumbar Fluid	Right	Left
Glioma	48	13	14	Glioma	116	8	11
Glioma	48	8	..	Glioma	138	12	18
Glioma	58	12	..	Neuroma	170	12	..
Glioma	59	7	..	Neuroma	206	..	16
Glioma	61	17	..	Neuroma	207	..	12
Glioma	61	..	11	Neuroma	222	19	..
Neuroma	61	..	8	Neuroma	235	..	51
Neuroma	63	10	10	Neuroma	246	13	14
Glioma	63	..	11	Neuroma	334	..	10
Glioma	73	73	..	Neuroma	396	8	13
Neuroma	73	44	..	Neuroma	400	13	13
Glioma	83	9	9	Neuroma	414	..	40
Glioma	106	8	14	Neuroma	450	11	..

TABLE 5.—*Comparison of the Protein Content of the Lumbar Fluid and That of the Ventricular Fluid in Twenty-Three Cases of Tumor of One Cerebral Hemisphere*

	Protein Content, Mg. per 100 Cc.				Protein Content, Mg. per 100 Cc.		
		Ventricular Fluid			Ventricular Fluid		
Type of Tumor	Lumbar Fluid	Homo-lateral	Contra-lateral	Type of Tumor	Lumbar Fluid	Homo-lateral	Contra-lateral
Tuberculoma	56	82	..	Glioma	93	55	..
Glioma	63	..	16	Glioma	100	87	..
Glioma	67	30	13	Glioma	112	138	17
Glioma	68	40	..	Glioma	118	306	35
Carcinoma	73	140	..	Glioma	140	112	..
Glioma	78	73	9	Meningioma	154	510	18
Glioma	78	..	20	Hemangioma	160	103	83
Glioma	80	180	56	Carcinoma	162	100	..
Glioma	82	30	25	Glioma	170	51	..
Glioma	82	3,060*	22	Glioma	204	150	..
Carcinoma	85	83	27	Glioma	336	726	73
				Glioma	354	156	10

* This value may represent the protein content of fluid from a cyst.

2. Cases in Which the Protein Content of the Lumbar Fluid Was Increased.—I have examined the ventricular fluid in 56 cases in which the protein content of the lumbar fluid was abnormal.

A. Tumor of the Posterior Fossa: In 26 cases of tumor of the posterior fossa the protein content of the lumbar fluid varied from 48 to 450 mg. The protein content of the ventricular fluid was less than 20 mg. in all but 4 cases, and in only 2 instances, more than 45 mg. The fluid in these cases contained 73 and 51 mg., respectively (table 4). In 9 other cases in which lumbar puncture was not done, the ventricular fluid contained less than 20 mg. of protein.

B. Tumor of the Cerebral Hemisphere: In table 5 is presented a comparison of the protein content of the lumbar fluid with that of the ventricular fluid in 23 cases of tumor of one cerebral hemisphere, in which the protein content of the lumbar fluid varied from 56 to 354 mg. The protein content of the fluid from the ventricle on the side of the tumor varied from 30 to 726 mg., and that of the fluid from the contralateral ventricle, from 9 to 83 mg. In only 4 cases the fluid from the contralateral ventricle contained more than 25 mg. of protein, and in each instance the fluid from this ventricle had a much smaller protein content than that of the fluid from the ventricle involved by the tumor. In 9 cases of tumor of one cerebral hemisphere in which lumbar puncture was not done, the protein content of the fluid from the homolateral ventricle varied from 57 to 522 mg. In 3 of these cases the fluid from the contralateral ventricle had a protein content of 13, 16 and 56 mg., respectively.

C. Tumor of the Corpus Callosum or Third Ventricle: In table 6 is shown a comparison of the protein content of the lumbar fluid with that of the ventricular in 7 cases of tumor of the corpus callosum or of the third ventricle. In 2 of these cases lumbar puncture was not done, but the findings in the ventricular fluid are so characteristic that they are presented.

TABLE 6.—*Comparison of the Protein Content of the Lumbar Fluid and That of the Ventricular Fluid in Seven Cases of Glioma of the Corpus Callosum or Third Ventricle*

	Protein Content, Mg. per 100 Cc.		
Location of Tumor	Lumbar Fluid	Fluid from Right Ventricle	Fluid from Left Ventricle
Corpus callosum	50	41	25
Corpus callosum	93	28	44
Third ventricle	438	..	135
Third ventricle	...	100	83
Third ventricle	510	156	162
Third ventricle	...	261	267
Third ventricle	684	342	318

An analysis of the data in this table shows that the protein content of the lumbar fluid varied from 50 to 684 mg. The protein contents of the fluids from the two lateral ventricles were approximately equal and varied from 28 to 342 mg.

In one case metastatic carcinomatous nodules were present in both cerebral hemispheres. The protein content of the fluid from the right ventricle was 258 mg., and that from the left, 82 mg.

COMMENT

The cerebrospinal fluid pressure is usually increased in cases of tumor of the brain. In this series normal pressures were common in cases of tumor of the brain stem or of the pituitary fossa and in those of glioma of a cerebral hemisphere with areas of cystic degeneration. Tumors located on the convexity of the hemisphere, especially meningiomas, may be accompanied by normal or only slightly elevated pressure, since such tumors do not interfere greatly with the circulation of the cerebrospinal fluid.

The cerebrospinal fluid was xanthochromic in 28 per cent of the cases. Xanthochromia was usually associated with a high protein

content. In a few cases the xanthochromia was due to destruction of red blood cells which had been extravasated by the tumor.

The cell count was usually normal in the lumbar cerebrospinal fluid. In 29 per cent of the cases there were more than 6 cells, and in only 17 per cent, more than 10 cells, per cubic millimeter. Pleocytosis in the cerebrospinal fluid was due in most cases to an aseptic meningeal reaction to necrosis of brain or tumor tissue near the ventricles. Most reported instances of marked pleocytosis in the cerebrospinal fluid have been cases of tumor of the frontal lobes involving the corpus callosum. Marked pleocytosis is occasionally found in cases of tumor in the region of the pituitary fossa. The pleocytosis in these cases is probably due to localized meningitis resulting from erosion of the nasal sinuses by the tumor.

The protein content of the lumbar fluid was elevated in cases in which the ventricular walls had been involved by the tumor and in cases of tumor in the posterior fossa. The increased protein content of the lumbar fluid in cases of tumor of the brain is apparently due to exudation from vessels in the tumor, and in those of tumor in the posterior fossa, to stagnation of the fluid in the lumbar sac. In cases of supratentorial tumor increased protein content was almost always observed when the tumor was in the corpus callosum or third ventricle. In cases of neuroma of the acoustic nerve an increased protein content of the lumbar fluid was almost constantly found, which was usually much higher than that of the fluid in cases of glioma of the cerebellum or fourth ventricle. It is probable that in cases of neurofibroma protein is more likely to be exuded into the fluid than in cases of cerebellar glioma.

The determination of the protein content of the fluid of the lateral ventricles and a comparison of the results with the protein content of the lumbar fluid are frequently invaluable in the localization of the tumor. In many cases the information thus obtained will obviate the necessity of a ventriculogram. This is especially true when the protein content of the lumbar fluid is increased.

In order to prevent the admixture of the fluid from the two lateral ventricles, the fluid should be withdrawn from the ventricles at the same time. Correction must be made for blood in the ventricular fluid. It is not necessary that the lumbar puncture be performed at the same time as the ventricular punctures. A satisfactory comparison can usually be obtained if the lumbar puncture is performed within from twenty-four to seventy-two hours before the ventricular punctures. Analysis of the protein content of the lumbar fluid or the ventricular fluid is of no value after the injection of air, since this is followed by aseptic meningitis.

The following conclusions derived from the findings in the cases in my series may be summarized: 1. When the protein content of the lumbar fluid is high and that of the fluid of both lateral ventricles is normal, the tumor is in the posterior fossa. The increased protein content of the lumbar fluid is due to exudation from the tumor in the posterior fossa and to stagnation of the fluid in the lumbar sac. 2. When the protein content of the fluid from the lumbar region and of that from both lateral ventricles is high, the tumor is in the third ventricle or the corpus callosum, or there are multiple (usually metastatic) tumors. 3. When the protein content of the fluid from the lumbar region and that of the fluid from one lateral ventricle is high, and that of the fluid from the other lateral ventricle is normal, the tumor is on the side in which the ventricular fluid shows the increased protein content, and the tumor extends deeply enough in the hemisphere to involve the ventricular wall.

DIFFERENTIAL DIAGNOSIS

The findings in the cerebrospinal fluid in cases of abscess of the brain are similar to those in cases of tumor of the brain. The chief aid in the differential diagnosis is the cell count of the fluid. In 75 per cent of cases of abscess of the brain but in only 17 per cent of those of tumor of the brain there are more than 10 cells per cubic millimeter in the lumbar fluid. Polymorphonuclear leukocytes are rarely found in the fluid in cases of tumor of the brain, while they usually constitute from 10 to 25 per cent of the total count in cases of abscess of the brain. In the rare cases of tumor of the brain with marked pleocytosis in the fluid, the differential diagnosis cannot be made on the basis of the cerebrospinal findings. The presence of a septic focus, such as chronic mastoiditis, osteomyelitis of the skull or abscess of the lung, favors the diagnosis of abscess of the brain.

The differential diagnosis of subdural hematoma and tumor of the brain usually cannot be made from the findings in the cerebrospinal fluid. A history of recent severe or minor injury of the head is important in such cases.[25]

In cases of cerebral hemorrhage frankly bloody cerebrospinal fluid is usually present.[26] Such fluids are rare in cases of tumor of the brain.

In cases of subarachnoid hemorrhage the fluid is frankly bloody at the onset, but if puncture is not performed until eight or ten days

25. Munro, D.: The Diagnosis and Treatment of Subdural Hematomata, New England J. Med. **210**:1145, 1934.

26. Aring, C. D., and Merritt, H. H.: The Differential Diagnosis Between Cerebral Hemorrhage and Cerebral Thrombosis, Arch. Int. Med. **56**:435 (Sept.) 1935.

after the hemorrhage the fluid may be only xanthochromic and under high pressure. In such cases subsequent punctures will show normal pressure. The pressure usually remains elevated in cases of tumor of the brain.

Cerebral thrombosis can usually be excluded by determination of the cerebrospinal fluid pressure and the protein content of the fluid. Pressures of more than 300 mm. are rare, and pressures higher than 400 mm. are not found in cases of cerebral thrombosis, unless complicated by uremia or congestive heart failure.[26] Such pressures are common in cases of tumor of the brain. A protein content of more than 100 mg. per hundred cubic centimeters is also uncommon in cases of cerebral thrombosis, whereas in 32 per cent of the cases of tumor of the brain in this series the protein content was higher than 100 mg.

Uremia can be excluded on the basis of the normal content of nonprotein nitrogen of the blood and cerebrospinal fluid in cases of tumor of the brain.

Epidemic encephalitis and multiple sclerosis can usually be excluded on the basis of the increased cerebrospinal fluid pressure.

Syphilis of the central nervous system is excluded by the normal cell count and by the negative Wassermann reaction of the cerebrospinal fluid. The Wassermann test should be repeated in the rare cases of tumor of the brain in which a false positive reaction is obtained.

Tuberculous meningitis is excluded by the normal cell count and sugar content of the fluid in cases of tumor of the brain. The chloride content of the fluids in cases of tumor of the brain is usually normal, and only rarely is the degree of reduction of chlorides observed that is common in cases of tuberculous meningitis.

SUMMARY

The findings in the cerebrospinal fluid in the lumbar fluid in 182 proved cases of tumor of the brain are presented.

An analysis of the ventricular fluid in 86 of these cases and in 19 other proved cases is presented. Data are given, showing that a comparison of the protein content of the lumbar fluid with that of the ventricular fluid can be of definite aid in the localization of the tumor.

PATHWAYS FOR PUPILLARY CONSTRICTION

LOCATION OF SYNAPSES IN THE PATH FOR THE PUPILLARY LIGHT REFLEX AND OF CONSTRICTOR FIBERS OF CORTICAL ORIGIN

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Among the fibers which pass from the retina are the afferent fibers of the pupilloconstrictor light reflex arc, for cutting the optic nerves abolishes the reactions of the pupils to light. The central course of the fibers concerned with this reflex was investigated in normal cats by Ranson and Magoun.[1] They reported that constrictor responses are obtained from stimulation of the optic chiasm, the optic tract on the lateral surface of the brain stem and ventral to the lateral geniculate body, the brachium of the superior colliculus, the pretectal region, the posterior commissure and the fibers emerging from it and arching ventrally around the central gray matter at the level of the transition between the third ventricle and the cerebral aqueduct and from the oculomotor nerve. Stimulation of the superior colliculus never produces constriction of the pupil.

In stimulation experiments on cats and monkeys Karplus and Kreidl[2] were able to follow the path of the light reflex centrad over the optic tract into the brachium of the superior colliculus and into the furrow at the anterior border of the superior colliculus, i. e., into the pretectal region. But when these workers stimulated the superior colliculus itself, dilatation of the pupil ensued. With the more refined technic made possible by the Horsley-Clarke instrument, Ranson and Magoun[1] showed that no response was obtained from the superior colliculus. However, when the electrode had penetrated to the underlying central gray matter of the aqueduct or into the tegmentum of the

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1. Ranson, S. W., and Magoun, H. W.: The Central Path of the Pupilloconstrictor Reflex in Response to Light, Arch. Neurol. & Psychiat. **30**:1193 (Dec.) 1933.

2. Karplus, J. P., and Kreidl, A.: Ueber die Bahn des Pupillarreflexes, Arch. f. d. ges. Physiol. **149**:115, 1913.

midbrain, stimulation caused dilatation of the pupil, except far rostrally, where fibers from the posterior commissure arch ventrally toward the Edinger-Westphal nucleus. Direct stimulation was repeatedly applied to the tectobulbar and tectospinal fibers which arch around the central gray matter to reach Meynert's decussation, but pupilloconstriction was never obtained from them. Stimulation of the tegmentum, which surrounds the central gray matter and contains these fibers, regularly yielded dilatation of the pupils.

In agreement with these findings is the repeatedly confirmed observation that the constrictor response to light remains intact after extirpation of the superior colliculus (Knoll,[3] Bechterew,[4] Ferrier and Turner,[5] Levinsohn,[6] Bernheimer,[7] Keller and Stewart [8] and Magoun [9]). A review of the literature on the afferent path of the light reflex is given in a paper by Magoun and Ranson.[10]

The constrictor responses of the pupil to stimulation of the optic chiasm and the optic tract are due to excitation of fibers of retinal origin. However, the pupilloconstriction obtained from stimulation of the brachium of the superior colliculus and the structures medial to it could be due to activation of fibers of retinal origin or of neurons with which these retinal fibers synapse. The present investigation was undertaken in the hope of determining whether the fibers of the optic nerve that are responsible for pupillary constriction run without interruption to the sphincter center for the pupil in the oculomotor nucleus or, if not, where the synapses are located. After degeneration of all the fibers of retinal origin no response should be obtained from stimulation of the optic chiasm or tracts, but if synapses exist, systematic stimulation along the known course of the pathway should yield constriction of the pupil from the nucleus which contains the synapses and from the

3. Knoll, P.: Beiträge zur Physiologie der Vierhügel, Beitr. z. Anat. u. Physiol. **4**:109, 1869.

4. Bechterew, W.: Ueber den Verlauf der die Pupille verengenden Nervenfasern im Gehirn und über die Localisation eines Centrums für die Iris und Contraction der Augenmuskeln, Arch. f. d. ges. Physiol. **31**:60, 1883.

5. Ferrier, D., and Turner, W. A.: Experimental Lesions of the Corpora Quadrigemina in Monkeys, Brain **24**:27, 1901.

6. Levinsohn, G.: Beiträge für Physiologie des Pupillarreflexes, Arch. f. Ophth. **59**:191 and 436, 1904; Experimentelle Untersuchungen über die Beziehungen des vorderen Vierhügels zum Pupillarreflex, ibid. **72**:367, 1909.

7. Bernheimer, S.: Weitere experimentelle Studien zur Kenntnis der Lage des Sphincter- und Levatorkerns, Arch. f. Ophth. **70**:539, 1909.

8. Keller, A. D., and Stewart, L.: The Superior Colliculus and the Pupillary Light Reflex in the Cat, Am. J. Physiol. **101**:64, 1932.

9. Magoun, H. W.: Maintenance of the Light Reflex After Destruction of the Superior Colliculus in the Cat, Am. J. Physiol. **111**:91, 1935.

10. Magoun, H. W., and Ranson, S. W.: The Afferent Path of the Light Reflex: A Review of the Literature, Arch. Ophth. **13**:862 (May) 1935.

fibers leading from this nucleus to the sphincter nucleus of the oculomotor nerve.

METHOD

Under aseptic conditions both optic nerves in a series of seven cats were severed between the optic foramen and the optic chiasm by a subtemporal approach from one side only. Cutting the optic nerves at this point avoided injury to the efferent mechanism of the pupilloconstrictor arc, i. e., the oculomotor nerve, the ciliary ganglion and the short ciliary nerves. The animals were kept for from twelve to forty-four days, and during that time each one was repeatedly examined for pupillary responses to light. Very bright lights flashed into the eyes failed to cause any pupillary constriction, and the animals gave every evidence of being totally blind. Subsequent microscopic study of serial sections of the chiasm and of the nerves showed complete transection of the optic nerves in all cases.

The stimulation was performed with the animal under light anesthesia induced by pentobarbital sodium. The region of the brain stem which was explored extended from the caudal portion of the diencephalon through the pretectal region to the rostral portion of the midbrain. The technic for systematic stimulation of the interior of the brain described by Ranson [11] and by Ranson and Magoun [1] was employed. With the Horsley-Clarke stereotaxic instrument, a bipolar electrode less than a millimeter in diameter and a weak faradic current, the appropriate part of the brain was explored by electrically stimulating in orderly succession every cubic millimeter of its substance. Subsequent microscopic examination of serial sections of the explored area made possible the anatomic identification of each point stimulated. The location of these points and the responses obtained from their stimulation were indicated on a standard series of drawings of transverse sections through the region. Separate charts of this character were prepared for each cat, and the results were summarized in the composite diagrams (figs. 1 *A* to *D*; 2 *A* and *B*).

RESULTS

The observations made in these experiments give information concerning the existence and location of synapses in the pathway for the pupillary light reflex and the location of fibers carrying constrictor impulses from the cerebral cortex.

The Location of Synapses in the Pathway of the Light Reflex.—A study was made of seven cats which were used from twelve to forty-four days after section of the optic nerves and in which no reactions were obtained from the optic tracts. In none of these animals was pupillary constriction ever obtained from stimulation of the lateral geniculate body. This is in accord with the generally accepted idea that this body is not concerned with the pupillary reflex. Marked constriction of the pupils was repeatedly obtained from stimulation of the pretectal area, in some instances when the tips of the electrodes merely rested on the dorsal surface of that part of the brain (fig. 1 *B* and *C*). Since in these cats the primary optic fibers had been stimulated in the optic tract and in

11. Ranson, S. W.: On the Use of the Horsley-Clarke Stereotaxic Instrument, Psychiat. en neurol. bl. **38**:534 (May-Aug.) 1934.

the superior quadrigeminal brachium without obtaining constrictor responses, the reactions obtained from the pretectal area must have been due either to activation of neurons of the second order with which the retinal fibers synapse in this region or to excitation of fibers from the cerebral cortex. The constrictions of the pupils in response to stimulation of the posterior commissure and the fibers passing from it around the central gray matter to the region of the Edinger-Westphal nucleus were just like those obtained in normal cats by Ranson and Magoun [1] and were often maximal, reducing the pupils to mere slits (fig. 1). There is evidence that a partial decussation of the fibers subserving the

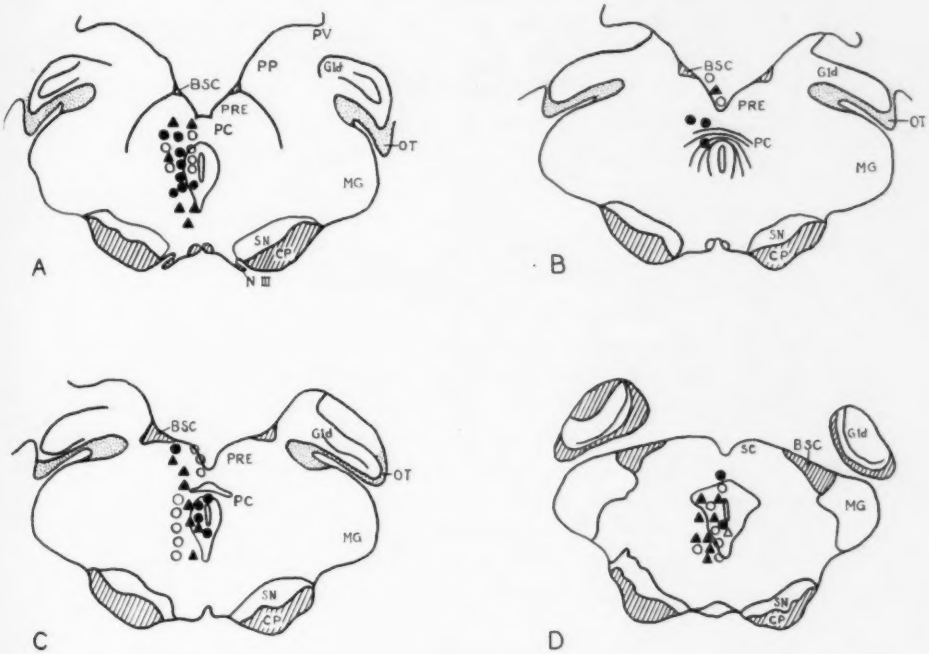

Fig. 1.—Diagrammatic representation of frontal sections of the cat's brain: *A*, through the posterior commissure, 0.7 mm. anterior to the level of *B*; *B*, through the posterior commissure; *C*, through the posterior part of the lateral geniculate body, and *D*, through the superior colliculus and the posterior end of the lateral geniculate body. Some of the white structures are cross-hatched, while the degenerated optic tracts are stippled. In this figure and in figure 2 the black dots represent the points stimulation of which yielded constriction of the pupils to slits; circles, the points stimulation of which yielded constriction of the pupils to one half or less of their previous diameter, and triangles, the points stimulation of which yielded only a slight constriction. *BSC* indicates brachium of the superior colliculus; *CP*, cerebral peduncles; *Gld*, dorsal part of the lateral geniculate body; *MG*, medial geniculate body; *NIII*, oculomotor nerve; *OT*, optic tract; *PC*, posterior commissure; *PP*, pulvinar posterior; *PRE*, pretectal area; *PV*, pulvinar; *SC*, superior colliculus, and *SN*, substantia nigra.

light reflex occurs in the posterior commissure. Spiegel [12] and Magoun, Ranson and Mayer [13] found a partial loss of the light reflex after destruction of the posterior commissure.

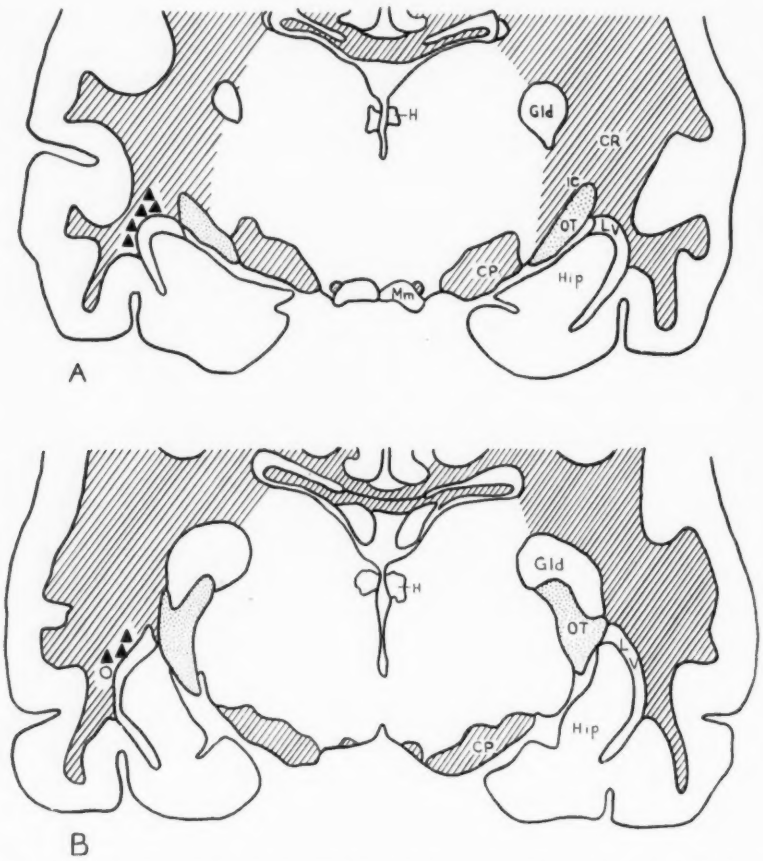

Fig. 2.—Diagrammatic representation of frontal sections of the cat's brain: *A*, through the rostral end of the lateral geniculate body; *B*, through the middle of the lateral geniculate body. Some of the white structures are cross-hatched; the degenerated optic tracts are stippled. *CP* indicates cerebral peduncle; *CR*, corona radiata; *Gld*, dorsal part of the lateral geniculate body; *H*, habenular nuclei; *Hip*, hippocampus; *IC*, internal capsule; *LV*, lateral ventricle; *Mm*, mamillary body, and *OT*, optic tract.

12. Spiegel, E. A.: Further Experiments on the Localization of the Argyll Robertson Phenomenon (Injuries to the Posterior Commissure), in Volume jubilaire en l'honneur du Prof. G. Marinesco, Bucharest, Société Roumaine de Neurologie, Psychiatrie et Endocrinologie, 1933, p. 625.

13. Magoun, H. W.; Ranson, S. W., and Mayer, L. L.: The Pupillary Light Reflex After Lesions of the Posterior Commissure in the Cat, Am. J. Ophth. **18**:624 (July) 1935.

Constrictor Fibers from the Cerebral Cortex.—In three cats weak constriction of the pupils (contractions from an initial diameter of 9 or 10 mm. to one of 7 or 8 mm.) was obtained on stimulation of the white matter in the dorsal and lateral walls of the lateral ventricle at the level of the rostral portion of the dorsal nucleus of the lateral geniculate body (figs. 2 *A* and *B*). The possibility that these responses of the pupils might have been due to spread of current to the adjacent optic tract becomes most remote in the light of the fact that repeated stimulation of the optic tract itself failed to cause any constriction.

Pupilloconstriction on stimulation of the cerebral cortex of part of the gyrus compositus posterior of the cat was reported by Wang, Lu and Lau.[14] This work has been repeated and confirmed in this laboratory by Barris.[15] This cortical area, which on electrical stimulation excites constriction of the pupils, was excised in several cats, and the brains were stained by the Marchi method. Degenerated fibers could be traced from the cortical lesion along the lateral wall of the lateral ventricle, over the lateral geniculate body and through the stratum zonale of the thalamus to the pretectal area. These degenerated cortical fibers are aggregated into a small fascicle in the wall of the lateral ventricle at that point which when stimulated in cats with the optic tracts degenerated yielded constriction of the pupils. The fibers become scattered as they pass through the stratum zonale of the thalamus to the pretectal area. It seems certain that the strong constriction of the pupils to slits obtained in the present investigation on stimulation of the pretectal area, the posterior commissure and the fibers arching ventrally from it toward the Edinger-Westphal nucleus could not be due to activation of these scattered cortical fibers which when stimulated in a bundle in the wall of the lateral ventricle yielded only a very weak constriction. These marked reactions must be due to the activation of neurons of the second order in the pathway of the pupillary light reflex.

COMMENT

In serial sections, stained by the Marchi method, of the brains of cats from which an eye had been enucleated, Barris, Ingram and Ranson[16] traced crossed and uncrossed fibers of retinal origin through the stratum zonale of the thalamus to the pretectal area, where they appeared to terminate. By the same method fibers from the cortex

14. Wang, G. H.; Lu, T. W., and Lau, T. T.: Pupillary Constriction from Cortical Stimulation, Chinese J. Physiol. **5**:205, 1931.

15. Barris, R. W.: A Pupilloconstrictor Area in the Cerebral Cortex of the Cat and Its Relation to the Pretectal Area, J. Comp. Neurol., to be published.

16. Barris, R. W.; Ingram, W. R., and Ranson, S. W.: Optic Connections of the Diencephalon and Midbrain of the Cat, J. Comp. Neurol. **62**:117 (Aug.) 1935.

have been followed to the pretectal area, where they too appear to end.[15] These anatomic indications that the pretectal area is the site of a synapse in the pathway concerned with constriction of the pupil are confirmed by the physiologic evidence of pupillary constriction on electrical stimulation of this region after degeneration of the optic tracts. That the pretectal region constitutes an important part of the light reflex pathway is shown by the fact that the response can be permanently abolished by the bilateral destruction of that region (Magoun and Ranson,[17] Magoun [9]). But the evidence so far available does not make it possible to decide which of the several groups of cells found in this region are concerned with the reaction.

This method of locating synapses by stimulation after degeneration of the afferent fibers is similar in principle to that used by Langley in the analysis of the sympathetic system. He used nicotine to block the preganglionic impulses at the synapses and then located the cells of origin and the course of the postganglionic fibers by direct stimulation. The absence of synapses anywhere between the cortex and the pons in the pathway for mastication and lapping was demonstrated by Magoun, Ranson and Fisher,[18] who showed that stimulation anywhere along this pathway was without effect after ablation of the appropriate cortical area. While applicable to only a limited number of problems, this method of locating synapses in the central nervous system after degeneration of the afferent fibers will from time to time be found useful.

SUMMARY

There are synapses in the path for the pupilloconstrictor reflex in response to light. These synapses are located in the pretectal region, but the results obtained do not make possible the identification of the particular group or groups of cells involved.

Constriction of the pupil was obtained from stimulation of the white matter in the lateral wall of the lateral ventricle at the level of the rostral part of the lateral geniculate body. It is believed that this constriction was due to stimulation of efferent fibers of cortical origin.

17. Magoun, H. W., and Ranson, S. W.: The Central Path of the Light Reflex: A Study of the Effect of Lesions, Arch. Ophth. **13**:791 (May) 1935.

18. Magoun, H. W.; Ranson, S. W., and Fisher, C.: Corticifugal Pathways for Mastication, Lapping and Other Motor Functions in the Cat, Arch. Neurol. & Psychiat. **30**:292 (Aug.) 1933.

THE FIBERS OF THE PUPILLARY REFLEX AND THE ARGYLL ROBERTSON PUPIL

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My attention has only recently been drawn to two papers on the Argyll Robertson pupil by Merritt and Moore,[1] of Boston, and Ranson and Magoun[2] in the ARCHIVES OF NEUROLOGY AND PSYCHIATRY. I propose to show that neither of these two schemes of the path of the fibers of the pupillary reflex is satisfactory, in that no proper provision is made for the consensual light reflex.

Merritt and Moore claimed that their explanation of the production of the Argyll Robertson pupil explains the phenomena better than any hitherto offered. They asserted that the lesion is just ventral to either side of the posterior commissure, involving both the light reflex fibers decussating in the posterior commissure and the sympathetic pathway.

As Merritt and Moore made no reference to a paper in which I[3] discussed the subject in *Brain* thirty years ago and in which I showed by experiments on cats that complete division of the posterior commissure had no permanent effect on the pupillary reflex, I assume that it must have escaped their notice.

As long ago as 1886 Darkshevich[4] propounded the theory of decussation of the fibers of the pupillary light reflex in the posterior commissure, and described the fibers as leaving the optic tract near the external geniculate body and passing through the thalamus to the ganglion habenulae and the pineal body, decussating in the posterior commissure with those of the other side to reach the upper oculomotor nucleus.

At the time that view of a decussation of the fibers of the pupillary light reflex in the posterior commissure greatly attracted me, as my studies of the pupillary reaction in birds showed that in them complete posterior decussation of these fibers is a necessary postulate (fig. 4). In order to test Darkshevich's theory, I therefore attempted to divide

1. Merritt, H. H., and Moore, M.: The Argyll Robertson Pupil: Anatomic-Physiologic Explanation of the Phenomenon, with a Survey of Its Occurrence in Neurosyphilis, Arch. Neurol. & Psychiat. **30**:357 (Aug.) 1933.

2. Ranson, S. W., and Magoun, H. W.: The Central Path of the Pupillo-constrictor Reflex in Response to Light, Arch. Neurol. & Psychiat. **30**:1193 (Dec.) 1933.

3. Harris, W.: Binocular and Stereoscopic Vision in Man and Other Vertebrates, with Special Reference to the Decussations of the Optic Nerves, the Ocular Movements and the Pupil Light Reflex, Brain **27**:107, 1904.

4. Darkshevich: Arch. f. Anat. u. Entwcklngsgesch., 1886, p. 249.

the posterior commissure in four cats, two of the operations being completely successful, as proved later by autopsy, at which the posterior commissure was found to be completely divided without any injury to the superior colliculus. In all four animals there was complete loss of the pupillary reaction to light immediately after the operation, though later the reaction returned, becoming completely normal.

I therefore discarded Darkshevich's theory of a decussation in the posterior commissure and was led to consider another possible path, namely Meynert's fountain decussation. The fibers of the pupillary light reflex undoubtedly pass from the retina to the superior colliculi, although it is still uncertain whether they are the fine fibers which Cajal described as originating in the gray matter of the superior colliculus and running peripherally to the retina or whether they originate in the retina and after a lesion of the optic nerve degenerate centrally toward the superior colliculi.

In preparations stained by the Marchi method, after enucleation of one eye in the cat, I demonstrated dense degeneration surrounding the external geniculate body and spreading onto the surface of the superior colliculus on each side, but no degeneration could be traced farther (fig. 2).

If the fibers of the pupillary reflex are the fine fibers described by Cajal as originating in the gray matter of the superior colliculi, they would not show any sign of central degeneration after injury of the optic nerve or tract. In either case it must be assumed that the gray matter of the superior colliculus is an intermediary stage in the relay of the reflex between the retina and the oculomotor nucleus. In that tegmental gray matter the impulses of the light reflex from both the crossed and the uncrossed fibers in the chiasma are merged, whence I consider they are relayed by the decussating fibers of Meynert's fountain semidecussation (or similar fibers) to the nuclei of the oculomotor nerves. Such merging in the gray matter of the superior colliculus of the impulses of the light reflex from the corresponding halves of the two retinas is necessary to explain the consensual pupillary reflex when one eye is shaded, in the absence of commissural fibers between the two sphincter pupillary nuclei of the third nerves.

Merritt and Moore [5] definitely stated that these fibers from the optic nerves pass with the brachium of the superior colliculus to the cephalad end of the superior colliculus. A portion of the fibers cross in the dorsal portion of the posterior commissure, while the remainder arch ventrally toward the nuclei of the oculomotor nerves. It is also clear from their diagram of this semidecussation [6] that they considered

5. Merritt and Moore,[1] p. 359.
6. Merritt and Moore,[1] p. 362.

that these fibers are continuous and are not relayed through cells in the tegmentum of the colliculus.

They also stated definitely in the caption of their diagram that "the light reflex fibers from the nasal halves of the retina, which cross in the optic chiasm, recross in the posterior commissure." If this were

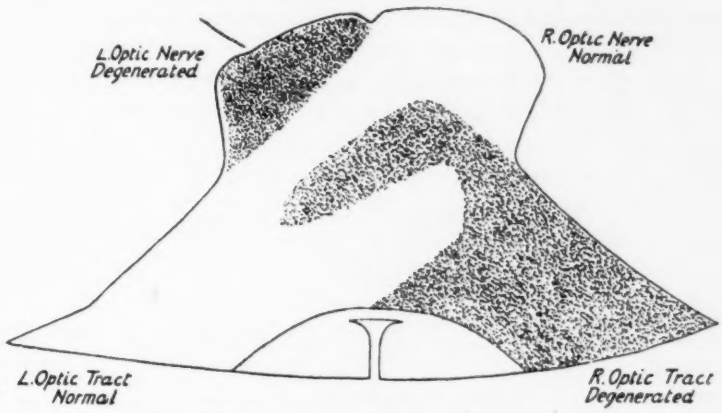

Fig. 1.—Optic chiasma of the pigeon, stained by Marchi's method, after enucleation of the left eye.

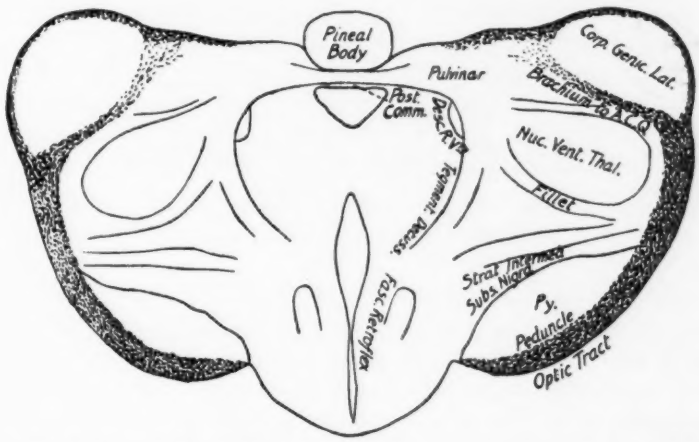

Fig. 2.—Section at the level of the posterior commissure of the cat, stained by Marchi's method, after enucleation of the left eye.

true, it is clear from their diagram that no consensual pupillary reflex would be produced on exposure of only one eye to light, except through commissural fibers between the two nuclei of the oculomotor nerves. The existence of such commissural fibers I have already shown to be impossible in birds and improbable in mammals.

Ranson and Magoun [2] stimulated electrically the posterior commissure in cats, with resulting constrictor responses of both pupils. From these results they argued that there is a partial decussation of the fibers of the pupillary light reflex in the posterior commissure and explained the fact that section of the posterior commissure does not produce any permanent effect on the pupils by assuming that there is also a secondary decussation of the fibers ventral to the central gray matter. That is to say, in part they agreed with the description of the path of the fibers of the pupillary light reflex which I published thirty years ago, with the exception that they denied the cell relay in the superior colliculus and assumed an additional semidecussation in the posterior commissure, which theoretically seems to me most unlikely. The pupillary constriction which they described as the result of electrical stimulation of the posterior commissure is, I think, explicable as due to an overflow of current, which would be carried by the fibers of the fasciculus retroflexus, another "Meynert's bundle," which runs from the ganglion habenulae on each side of the posterior commissure, crossing in the commissure and sweeping around the central gray matter to reach the interpeduncular ganglion of the opposite side. On the way to this ganglion the fibers pass close to the nuclei of the third nerves, and it is easy to understand how they might carry a current which would overflow to the pupillary constrictor centers in the nuclei. This was the path by which Darkshevich said that the fibers of the pupillary light reflex reach the nuclei of the oculomotor nerves.

Since my experiments proved that division of the posterior commissure in cats does not affect the reflex action of the pupil to light for more than a few days (the temporary loss being easily accounted for by shock to the neighboring superior colliculus), it seemed to me certain that the path from the superior colliculus to the nucleus of the third nerve must lie ventral to the aqueduct, and such a path is provided by the fountain decussation of Meynert.

In four of the cats in which I wounded the superior colliculus and in which the wound was deep enough to injure the tegmentum surrounding the central gray matter, I later found a well marked degeneration of Meynert's fountain decussation, sweeping from the level of the wound ventrally beneath the nucleus of the third nerve and the posterior longitudinal bundle, the majority of the fibers decussating in the raphe and then turning caudad to form a tract running longitudinally and ending in the fibers of the anterior columns of the spinal cord.

In my paper, read before the Neurological Society of London in December 1899, when I showed my sections and described my experiments, I suggested that some of these fibers contain the relay for the pupillary light reflex to the nuclei of the third nerves. My sections

showed, as Boyce previously stated, that not all of these fibers decussate, a few running caudad in the posterior longitudinal bundle of the same side. That tract, therefore, would provide the path for a posterior semidecussation of the fibers of the pupillary light reflex, which comparative studies of the pupils in birds and mammals show to be a necessary anatomic structure in mammals. The fountain decussation of Meynert must not be confused with the "superior commissure of Meynert," which lies dorsal to Gudden's commissure beneath the third ventricle, or with the bundle already referred to as the "fasciculus retroflexus," which connects the ganglion habenulae with the opposite interpeduncular ganglion.

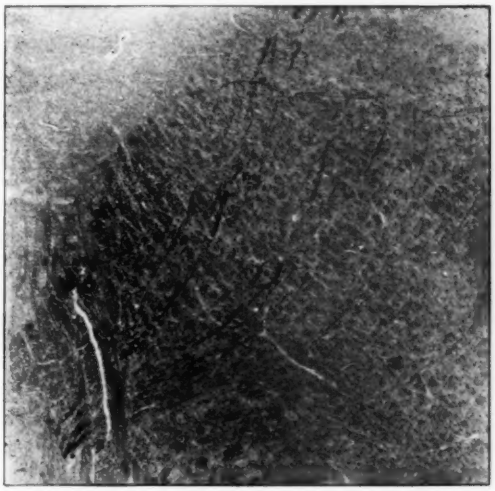

Fig. 3.—Photomicrograph showing degenerated fibers of Meynert's fountain decussation of a cat, stained by Marchi's method, after a wound of the superior colliculus.

I reproduce here (figs. 4 and 5) the two diagrams from my paper published in 1904, illustrating the probable path of the fibers of the pupillary reflex in birds and in higher mammals. In mammals Meynert's fountain decussation is shown, for the sake of simplicity, as originating as one fiber from the tegmental cell in the superior colliculus and then splitting into the semidecussation ventrally to the aqueduct to reach the nuclei of the third nerves; and I [7] stated in the earlier paper my opinion that the lesion that produces the Argyll Robertson pupil is sclerosis of these fibers, especially of their terminations in the neighborhood of the nuclei of the third nerves, and that

7. Harris,[3] p. 146.

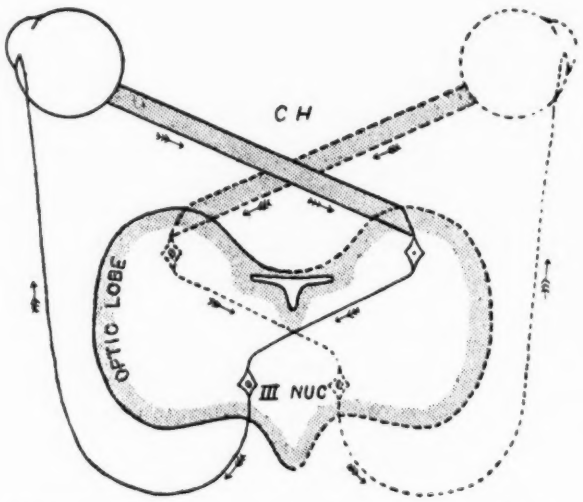

Fig. 4.—Diagram of the path of the pupillary reflex to light in birds, reptiles and some lower mammals.

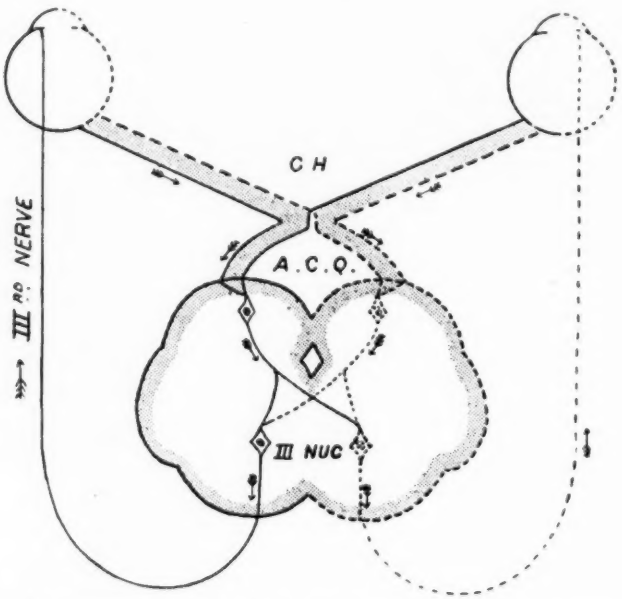

Fig. 5.—Diagram of the path of the pupillary reflex to light in man and other higher mammals.

in the case of a dilated type of Argyll Robertson pupil, which reacts neither to light nor in accommodation, it is probable that there is also a lesion affecting the anterior portions of the nuclei of the third nerves. In conclusion I stated:

"The typical form of Argyll Robertson pupil is minutely contracted, due no doubt to additional sclerosis of the sympathetic dilator nerve fibers with some additional contracture of the muscle of the sphincter iridis, due to the loss of the tonic dilator stimuli of the sympathetic."

Merritt and Moore did not refer to the extremely minute contraction of the pupil which is typical of the Argyll Robertson phenomenon. The extremely small size of the pupil is not to be explained by a loss of the pupillary reflex to light alone, combined with a loss of the dilator action of the sympathetic innervation. Moreover, in discussing the causation of the Argyll Robertson pupil they omitted to mention recovery following a lesion of the third nerve. I have seen a typical medium-sized or small Argyll Robertson pupil as a late result of a partial lesion of the third nerve resulting from a fracture of the base of the skull and from injection of alcohol into the foramen rotundum, in which all the ocular movements and diplopia had been recovered. Babinski [8] was fully aware of this result of partial lesions of the third nerve.

I [9] further stated that in carefully testing each half of a uniocular Argyll Robertson pupil with a pencil beam of light thrown from each lateral direction, I found in every case equally brisk consensual contraction of the opposite pupil, whichever half of the retina of the affected eye was illuminated. This point seems definite proof that consensual reaction of the pupil cannot be due to any intercommissural fibers between the anterior portions of the nuclei of the third nerves but must be due to a posterior semidecussation of the pupillary fibers between the superior colliculus and the nuclei of the third nerves.

My studies of the pupillary reflex in birds showed that there must be a complete posterior decussation of the fibers of the pupillary reflex to light, as there is no consensual pupillary reflex to light in birds and the optic nerves decussate completely at the chiasma.

In mammals, with semidecussation of the optic nerves (fig. 5), a consensual pupillary light reflex develops, which is best seen in cats, monkeys, apes and man.

Anatomically, therefore, it seems probable that in mammals there is a similar semidecussation of the fibers of the pupillary light reflex posteriorly in the region of the superior colliculus. If the posterior semidecussation of these fibers is, as asserted by Merritt and Moore

8. Babinski, J.: Personal communication to the author.

9. Harris,[3] p. 145.

and Ranson and Magoun, by the path of the posterior commissure, without being first relayed through cells in the superior colliculus, then anteroposterior section of the optic chiasma would at once abolish the consensual pupillary reflex. Experimental section of the chiasma in mammals, however, has been shown not to interfere with the pupillary light reflex, and clinical studies of cases of blindness due to tumors of the pituitary body confirm this point. In cases of bitemporal hemianopia due to pituitary lesions the consensual pupillary reflex remains unaltered; more convincing still is the persistence of the consensual pupillary reflex in those cases in which one eye is totally blind and only the nasal field of the other eye remains.

These facts are clear proof that there must be a fusion of the pupillary light impulses in the gray matter of the superior colliculus and that the semidecussation of the fibers starts from that point. My experiments of wounding the gray matter of the colliculus indicate a possible path for this semidecussation, viz., Meynert's fountain decussation; at the same time, it should be noted that no degenerated fibers could be traced into the posterior commissure as the result of the wound in the colliculus. To my mind a strong argument against the route through the posterior commissure for the fibers of pupillary light reflex and in favor of the subaqueductal decussation, as in Meynert's fountain bundle, is offered by the facts of comparative anatomy. The optic nerve in birds decussates completely at the chiasma and ends in the opposite optic lobe (fig. 4), the homolog of the superior colliculus in mammals. Thence, the light reflex pathway must cross totally to the nucleus of the opposite third nerve, and the most obvious route is clearly subaqueductal and not by way of the dorsal commissure.

An interesting experiment would be to divide the dorsal commissure between the optic lobes in pigeons and, if the birds can be kept alive sufficiently long, to observe the effects, if any, on the pupillary reflex. If the fibers of the light reflex cross by this dorsal route, then total loss of the pupillary reflex in both eyes should occur. Another interesting experiment in pigeons would be to wound the optic lobe on one side sufficiently deeply and subsequently to trace any Marchi degeneration to determine whether any totally decussating fibers cross ventrally to the aqueduct toward the region of the nuclei of the third nerve. Unfortunately, I cannot now attempt such experimental work myself, and a well known physiologist who attempted the experiments for me was unable to keep the birds alive.

SUMMARY

1. Merritt and Moore's scheme of the path of the fibers of the pupillary reflex does not explain the normal consensual pupillary reflex to light.

2. Ranson and Magoun, by a further splitting of the decussating pupillary fibers, accounted for the consensual pupillary reflex at the expense of a wholly improbable and fantastic arrangement of the fibers. Even that scheme, however, fails to account for the preservation of the consensual pupillary reflex after anteroposterior section of the optic chiasma or in the cases of bitemporal hemianopia due to a tumor of the pituitary body.

3. No scheme of the pathway of the fibers of the pupillary reflex will explain the various phenomena unless it accepts a fusion of the light impulses in the superior colliculus, whence they are forwarded by means of a semidecussating pathway to the nuclei of the third nerves.

SPONTANEOUS PAIN AND OTHER SUBJECTIVE SENSORY DISTURBANCES

A CLINICOPATHOLOGIC STUDY

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The types of sensation described as "hyperaffectivity," "hyperpathia," "central pain," "spontaneous pain" and "dysesthesia" have been the topic of many contributions. All of these sensations were first described by Dejerine [1] as forming the *syndrome thalamique*, and the subject was elaborated on later by his pupil Roussy [2] in the well known monograph entitled "La couche optique." According to Roussy the syndrome is characterized by "spontaneous pain," hemianesthesia, little or no hemiplegia, hemiataxia and choreo-athetoid movements. Of these symptoms "spontaneous pain" has received the most consideration. Head and Holmes [3] and others have shown that the acute paroxysmal pains, frequently intolerable and not amenable to any form of treatment, are caused by lesions of the lateral nucleus of the thalamus. The other symptoms are produced by lesions in the structures adjacent to the thalamus.

In 1911 Head and Holmes expressed the belief that "the feeling tone of somatic or visceral sensation is the product of thalamic activity" and that "this control is effected by means of paths from the cortex to the thalamus which probably end in the lateral nucleus of the thalamus." They stated that destruction of the cortex alone could not cause "spontaneous pain." Later, however, "spontaneous pain" associated with lesions of the peripheral nerves, spinal cord, bulb, pons, thalamus and cortex was described. The theories attributing the origin of "spon-

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Read before the meeting of the Association for Research in Nervous and Mental Disease, Dec. 28, 1934.

1. Dejerine, J.: Le syndrome thalamique, Rev. neurol. **14**:521, 1906.

2. Roussy, G.: La couche optique, Thèse de Paris, Paris, G. Steinheil, 1907.

3. Head, H., and Holmes, G.: Sensory Disturbances from Cerebral Lesions, Brain **34**:102, 1911; Studies in Neurology, New York, Oxford University Press, 1920. Holmes, G.: Disorders of Sensation Produced by Cortical Lesion, Brain **50**:413, 1927.

taneous pain" to cortical lesions have been most severely criticized. Head and Holmes contended that destruction of the cerebral cortex does not change the "threshold to measurable painful or uncomfortable stimuli" and affects only slightly the appreciation of temperature. Mills,[4] Piéron,[5] Marie and Bouttier,[6] Foerster[7] and others have expressed the opinion that these types of sensation can arise from cortical stimulation and irritation and can be disturbed by destructive lesions.

The present clinicopathologic presentation is concerned with the variable subjective types of sensation, such as "spontaneous pain" and other disagreeable sensations, including coldness, burning, "pins and needles," "feelings of electricity" and their structural correlates. An attempt is made, whenever possible, to interpret these sensations on a physiopathologic basis. From this presentation we have excluded the numerous types of subjective sensory disturbances due to psychogenic factors.

For this purpose eleven cases in which autopsies were performed were studied. The lesions were distributed as follows: one in the peripheral nerves, four in the spinal cord, four in the thalamus and two in the cortex. The types of subjective sensation associated with disease of the medulla oblongata and the pons are described briefly, since we wish to limit our discussion to cases in which the neural structures were available for histopathologic studies. We believe that our presentation is of special significance because two of our cases in which cortical lesions were present shed additional light on the subject of sensory representation in the cortex.

METHODS

Blocks from the areas of destruction, as well as above and below them, were embedded in pyroxylin and stained by the myelin sheath and cresyl violet methods. In the cases of thalamic and cortical lesions sections were cut serially, and every tenth section was stained by the same method. Thus we were able to determine the extent of the lesions of the ascending and descending degeneration and of additional lesions which may have caused the symptoms.

4. Mills, C. K.: Autopsy on a Case of Athetoid Spasm, Myotonia, and Diffuse Bilateral Disturbances of Sensation; Chronic Convexity Meningitis of Both Hemispheres with Cortical and Subcortical Softening; Lesions Most Marked in the Posterior Parietal Region, J. Nerv. & Ment. Dis. **18**:794, 1891.

5. Piéron, H.: Le cerveau et la pensée, Paris, Félix Alcan, 1923.

6. Marie, P., and Bouttier, H.: Etudes cliniques sur les modalités des dissociations de la sensibilité dans les lesions encéphaliques, Rev. neurol. **29**:1, 1922.

7. Foerster, O.: Die Leitungsbahnen des Schmerzgefühls und die chirurgische Behandlung der Schmerzzustände, Berlin, Urban & Schwarzenberg, 1927.

LESIONS AT THE PERIPHERAL LEVEL

The occurrence of spontaneous sensations in cases of lesion of a peripheral nerve is well known. The most common causes of "spontaneous pain" in this group are those caused by injuries to the peripheral nerves that produce the well known phenomenon that was described by S. Weir Mitchell as causalgia. This pain varies in intensity. It may be merely a burning or a very excruciating pain. It occurs mostly in the foot or hand along the course of the sciatic and median nerves. It is to be emphasized that causalgia seldom appears when the nerve is cut completely; it occurs after an incomplete injury of a peripheral nerve when the physiologic continuity of the nerve has been affected minimally. Objective sensation, although difficult to test because of the hyperaffectivity, may appear intact. Hypalgesia and hypesthesia or hyperalgesia and hyperpathia may be encountered. Causalgia is most likely sympathetic in origin, as evidenced by the emotional response to stimulation and the associated vasomotor disturbances.

Allied subjective sensory disturbances are the acroparesthesias commonly observed in women exhibiting early arteriosclerotic changes, acro-asphyxia, acrodynia, Raynaud's disease, scleroderma, dermatomyositis, intermittent claudication, trigeminal neuralgia and the condition observed after injections into the trigeminal and other nerves or the gasserian ganglion. These sensations are described as burning, swelling, cold or wet. One of our cases in which autopsy was performed illustrates this:

CASE 1.—*Neurofibroma of the cerebellopontile angle on the right side compressing the fifth, seventh and eighth cranial nerves. Burning sensations along the distribution of the right trigeminal nerve accompanied by objective sensory changes.*

History.—J. S., a woman aged 45, who was admitted to the Montefiore Hospital on Jan. 11, 1929, in 1925 first experienced a constant burning sensation over the right side of the face, inside of the cheek and on the right side of the gums, tongue and lips. When touched she experienced a sensation of freezing Extraction of the teeth brought no relief. There were a sticking feeling and a throbbing pain in the right eye and in the right side of the head associated with tearing of the right eye. Tinnitus was occasionally present for the same period. In 1928 dimness of vision was noted. This was followed by total loss of hearing.

Neurologic Examination.—In 1928 bilateral papilledema, deviation of the jaw to the right, disturbances of all modalities of sensation in the distribution of the right fifth nerve, palsy of the right facial nerve, nerve deafness in the right ear and a questionable Babinski response on the left side were observed.

Course.—The patient was operated on by Dr. Cushing on Nov. 30, 1928. A small tumor was found deeply embedded in the right cerebellopontile angle, which proved to be a neurofibroma of the acoustic nerve. Only a small portion of the growth was removed. The burning sensations of the left side of the face persisted.

Autopsy.—A firm tumor was present in the cerebellopontile angle on the right side, situated below the trigeminal nerve and impinging on it. The nerve had assumed a horizontal (fig. 1) position and was pushed against the cerebellum. The neoplasm was firmly attached to the auditory nerve and also compressed the facial nerve and the pons.

Comment.—Of interest in this case were the subjective sensory disturbances manifested by a burning sensation over the right side of the face, lips, mouth, gums and tongue due to a neurofibroma which irritated the sensory fibers of the trigeminal nerve at their exit from the pons.

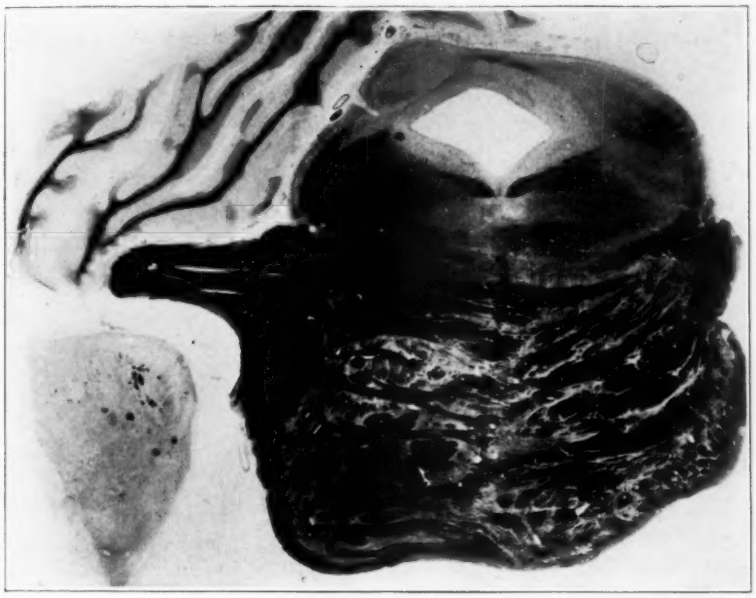

Fig. 1 (case 1).—Neuroma of the acoustic nerve situated below the trigeminal nerve and compressing and pushing it against the cerebellum. Myelin sheath stain.

LESIONS AT THE SPINAL LEVEL

"Central" or "spontaneous pain" and other subjective sensory disturbances may be encountered in cases of disease or injury of the spinal cord (Holmes [8]), syringomyelia (Haenel [9]; Dejerine and Thomas [10];

8. Holmes, G.: Spinal Injuries of Warfare, Brit. M. J. **2**:769, 1915; in Contributions to Medical and Biological Research, dedicated to Sir William Osler, New York, Paul B. Hoeber, Inc., 1919, vol. 1, p. 235.

9. Haenel, H., in Lewandowsky, M.: Handbuch der Neurologie, Berlin, Julius Springer, 1911, vol. 2, pt. 1, p. 587.

10. Dejerine, J., and Thomas, A.: Traité des maladies de la moelle épinière, Paris, J. B. Baillière et fils, 1902.

Taylor, Greenfield and Martin[11]; Raymond and Lhermitte,[12] and Spiller[13]), intramedullary and extramedullary neoplasms, multiple sclerosis, subacute combined degeneration and various myelopathies. Pain due to a lesion of the spinal cord must be differentiated from that due to irritation of the posterior roots and ganglia. "Central pain" is most likely produced by irritation of the spinothalamic pathways. Head and Holmes expressed the belief that it is due to removal of the inhibitory control which the cerebral cortex normally exerts on the subcortical centers concerned with the perception of this form of sensation. Spiller and others stated that hyperpathia is caused by irritation of the sensory tracts.

Four cases of disease of the spinal cord were selected to illustrate these peculiar sensory disturbances.

CASE 2.—*Cerebellar medulloblastoma with metastases to the spinal cord, involvement of the spinothalamic tracts in the dorsal segment and slight implication of the posterior columns in the region of the cervical enlargement. Severe "spontaneous pain" elicited by all types of stimuli and impairment of all forms of superficial sensation below the level of the lesion.*

History.—A. G., a man aged 28, was admitted to the hospital on Dec. 5, 1932, with the history that in February 1932 his head was injured in an automobile accident. Two weeks later he began to have projectile vomiting, and thereafter he lost a great deal of weight. In August 1932 he complained of dizziness and headache and noticed that his eyes were crossed. Following a convulsion, suboccipital craniotomy was performed, and a cerebellar medulloblastoma was partially removed. Later the patient received high voltage roentgen therapy.

Neurologic Examination.—On admission the gait was unsteady. The head, neck and torso moved like one rigid mass. The facies was fixed. Speech was slow, hesitant, monotonous and stammering. There was weakness of the right external rectus muscle.

Course.—On June 17, 1933, the patient complained of agonizing pain in the left half of the trunk, aching and "breaking-bone" pains in both shoulders, throughout the body and in both lower extremities. The pain was increased with every movement and manipulation, no matter how gentle. Neurologic examination at that time, in addition to the previous observations, disclosed flaccid paralysis, with bilateral signs referable to the pyramidal tracts and absence of the reflexes in the lower portion of the abdomen. On the left side a sensory level was present at the fourth thoracic segment, and on the right side there seemed to be a similar level at the third lumbar dermatome. Below these levels pinprick was felt as a sharp, intensely disagreeable pain radiating in all directions for a distance of about a foot

11. Taylor, J.; Greenfield, J. S., and Martin, J. P.: Two Cases of Syringomyelia and Syringobulbia Observed Clinically Over Many Years and Examined Pathologically, Brain **45**:323, 1922.

12. Raymond and Lhermitte, quoted by Oppenheim, H.: Textbook of Nervous Diseases, Edinburgh, O. Schulze & Co., 1911, vol. 1, p. 380.

13. Spiller, W. G.: Central Pain in Syringomyelia and Dysesthesia and Overreaction to Sensory Stimuli in Lesions Below the Optic Thalamus, Arch. Neurol. & Psychiat. **10**:491 (Nov.) 1923.

(30 cm.) or more, but not across the midline. One pinprick was perceived as ten or a hundred or more pricks, with other disagreeable associated sensations that radiated widely in all directions. When the tips of the hair were touched lightly, the patient felt as though he was being rubbed with a rough turkish towel. Pulling of the hair was intensely disagreeable to him and was diffusely perceived. Below the third dorsal segment on the left side the patient could not evaluate sensations of temperature properly. When a test tube of hot or cold water was applied first on the right and then on the left side of the body below the level of the lesion, the patient invariably said that it was hotter or colder on the left side. Cold and intense forms of heat also caused an acutely disagreeable feeling as painful as a toothache. This was present to a lesser degree in the right leg. If the bare skin in the affected dermatomes was stroked lightly with cotton-wool, the patient complained of roughness and a disagreeable deep pain like that of a "bone ache." If the deep tissues were stroked firmly or a bone anywhere below the shoulders was tapped or pressed on, the patient experienced an intolerable ache that made him cry. The hyperpathia was absent in the sacral zones. There was no impairment of sensation in the posterior columns, but vibrations of a tuning fork were perceived in the right ankle and in the left half of the body below the third dorsal segment as painful. When he clenched the left hand, a severe, sharp pain shot up the forearm to the elbow. Movements of the left shoulder caused pains to shoot up and down the left arm. Four months later the hyperaffective responses and sensory disturbances were evident on the left side of the perianal region. At no time was there radiation across the midline. The hyperpathia continued throughout the course of the illness. High voltage roentgen therapy gave slight relief, as did morphine. Spinal puncture revealed almost complete block; the fluid showed xanthochromia, gave a 4 plus Pandy reaction and contained 100 lymphocytes per cubic millimeter and 611 mg. of protein per hundred cubic centimeters. Other laboratory data were normal.

Autopsy.—A hemorrhagic medulloblastoma replaced the greater part of the right and part of the left cerebellar hemisphere. In sections through the fourth ventricle and medulla oblongata, invasion and destruction of the cerebellum, part of the brachium pontis and dentate nucleus, the tuberculum acusticum, the vestibular nuclei, the nuclei of the tenth and twelfth nerves and part of the corpus restiforme on the right side were observed. In sections of the medulla oblongata in the region of the nucleus of the eleventh nerve there was invasion of part of the nuclei graciles and cuneati by the neoplasm. The right pyramid at some levels also was invaded by the tumor. The spinothalamic components were preserved throughout all these segments.

Spinal Cord: A small tumor had compressed and destroyed part of the posterior columns in a section through the cervical enlargement (fig. 2*A*). In a section through the first dorsal segment there was tumor tissue on the lateral parts of the spinal cord implicating parts of the dorsal and ventral cerebellar, the spinothalamic and rubrospinal and part of the pyramidal tracts on the right side (fig. 2*B*). The spinal cord between the fourth and seventh dorsal segments was markedly distorted, and the greatest amount of demyelinization and destruction was observed in the lateral pyramidal and spinothalamic tracts. The posterior columns were fairly well spared.

Comment.—Of interest in this case were the severe central pain and the relative preservation of sensibility to pinprick below the level of the lesion during the early course of the illness. Later sensibility to

pinprick became definitely impaired. Heat and cold could not be evaluated properly and were perceived as sensations that radiated throughout the left half of the body and provoked an intensely disagreeable feeling, which seemed to be as painful as a toothache. When the affected dermatomes were stroked lightly with cotton-wool, the patient complained of a feeling of roughness and a disagreeable pain like that of a "bone ache." Sensation referable to the posterior column showed no changes except for vibratory stimuli, which were perceived

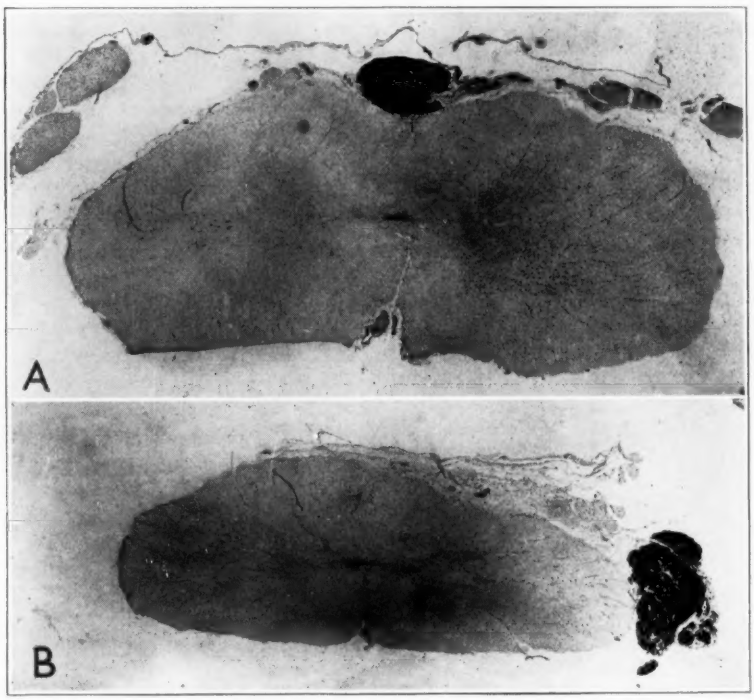

Fig. 2 (case 2).—*A*, tumor compressing and destroying part of the posterior columns in the region of the cervical enlargement. *B*, tumor situated laterally and compressing the spinothalamic tracts in the region of the first dorsal segment. Cresyl violet stain.

as painful in the right ankle and in the left half of the body below the third dorsal segment.

Histopathologic examination showed that the spinothalamic pathways were partly involved, approximately between the fourth and the sixth dorsal segment. The spinothalamic fibers in the medulla oblongata were spared. In addition, some tumor tissue invaded to a slight degree the posterior columns in the region of the cervical enlargement. Whether that lesion was responsible for the painful sensation produced

by vibration is more difficult to state. In this connection it is worth mentioning that Holmes also noticed that some of his patients experienced painful and unpleasant sensations with vibratory stimuli. Because of that he expressed the opinion that the posterior columns might have been partly responsible for the pain, although he considered the possibility of spinothalamic involvement. Foerster recorded similar cases. His contention that there are pain fibers within the posterior columns suggests a possible explanation for these hyperaffective responses. Most likely the hyperaffectivity in our case was caused by the lesions in the spinothalamic tracts.

CASE 3.—*Tuberculoma of the ninth dorsal segment. Subjective sensory disturbance of burning elicited by pinprick; vibratory, electric-like sensation produced by thermal stimuli.*

History.—A. C., a man aged 41, who was admitted to the hospital on Aug. 17, 1929, with a history of pulmonary tuberculosis since January 1929, in July 1929 experienced weakness of the legs and shortly thereafter complete paraplegia and loss of sphincteric control. Two weeks before admission he complained of paresthesia and pains in the lower extremities from the toes to the thighs.

Physical Examination.—Marked emaciation and physical signs of bilateral fibrocaseous pulmonary tuberculosis and cavitation were noted.

Neurologic Examination.—There was flaccid paraplegia with bilateral signs of involvement of the pyramidal tracts in the lower extremities. Analgesia, marked hypesthesia and thermohypesthesia were noted below the twelfth dorsal segment. The sense of touch was more impaired on the right side, and that of temperature, more on the left side. Vibratory sensibility was lost from the toes to the hips, and the postural sense was severely impaired in the toes, ankles and knees. Pinprick on the right side was experienced as a diffuse burning sensation which extended from the point stimulated down to the sole of the foot. On the left side pinprick was felt as a touch up to the twelfth dorsal dermatome. The dragging of a pin over the skin on the right side was experienced as a burning sensation in the entire area up to the twelfth dorsal dermatome, and on the left side the same stimulus induced a "feathery" sensation without pain. Sensibility to the touch of cotton-wool was slightly impaired but did not give rise to disagreeable sensations. When heat slightly warmer than the temperature of the skin was applied to the left side of the body below the level of the lesion, it gave rise to vibrating, electric-like sensations with no associated sensation of warmth. When a warm test tube was put first on a normal area of skin and then on the involved area, the patient detected sometimes a warm and sometimes a cold feeling. When cold was applied only to the affected left side of the body, it gave rise to the same sensations as did heat, i. e., vibrating, electric-like feelings with a frequently associated disagreeable affect. When cold was applied first to a normal area and then to the upper part of the diseased area, it was recognized for a short interval and then was called warm. The sensation was diffuse and not localized, regardless of the pressure applied. The same features were noticed in all tests with cold below the twelfth dorsal segment on the right side. When the sole of the foot was tested, an icy sensation radiated to the knee. These tests gave the patient a painful thrill that ran through the entire body.

Autopsy.—At the ninth thoracic segment of the spinal cord, on the anterior surface, there was a firm oval nodule measuring 2.5 by 0.5 cm. It was freely movable in the subarachnoid space for a distance of about 5 cm. Below the ninth dorsal segment the pia-arachnoid was adherent to the spinal cord. From this area down to the lumbar region the spinal cord appeared to be mushy. In sections stained for myelin sheaths the segments of the spinal cord from the tenth dorsal to the second lumbar showed complete destruction of the anterolateral columns, which were compressed by a tuberculoma (fig. 3). The anterolateral tracts, incuding the spinothalamic tracts as well as parts of the posterior columns, were destroyed by the tuberculoma. The posterolateral surface of the cord was the seat of an inflammatory process. The posterior roots were spared.

Comment.—In this case the striking feature was the nature of the disturbance in the subjective sensations produced by pain and tempera-

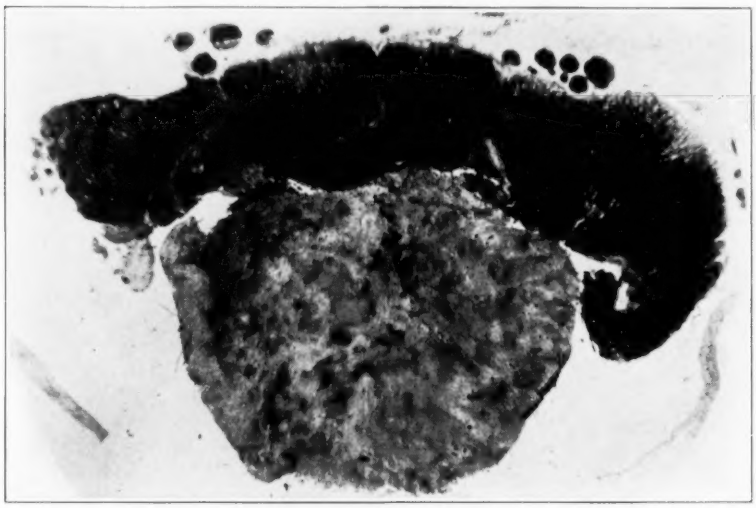

Fig. 3 (case 3).—Tuberculoma destroying the anterolateral tracts of the spinal cord, with implication of the spinothalamic tracts. Myelin sheath stain.

ture stimuli. Pinprick and the dragging of a pin gave rise to a burning sensation on the right but not on the left side. The application of heat produced vibratory, electric-like sensations on the left side. Cold applications gave similar reactions, but with that test the disagreeable affect was present bilaterally.

S. A. K. Wilson [14] stated that "in some cases a subjective thermal dysesthesia exists with loss of all thermal appreciation, in others it is present though no objective sensory change can be elicited." In this

14. Wilson, S. A. K.: Dysesthesiae and Their Neural Correlates, Brain **50:** 428, 1927.

case subjective thermal dysesthesias existed with only partial loss of thermal appreciation when the test tube was passed from above downward or from the normal to the diseased area, while no sensation of warmth or coldness was noted when the test object was applied only to the diseased area. We are inclined to attribute these phenomena to disease of the spinothalamic pathways that were involved bilaterally.

CASE 4.—*Diffuse toxic myelopathy. Sensory level below the third lumbar segment. "Spontaneous pain" and overreaction to pinprick; subjective disturbances of thermal sensibility, cold stimuli being called hot below the fourth lumbar segment.*

History.—D. G., a man aged 52, was admitted to the hospital in October 1928 with complaints of weakness and numbness of the lower extremities, pain in the lumbar portion of the spine radiating to the lower extremities and loss of vesical and rectal control. In September 1926 he experienced a continuous dull pain in both knees and difficulty in walking. In July 1928 he received several injections of neoarsphenamine. After the third injection hiccup, fever, chills, paralysis and sensory disturbances of the lower extremities, pain in the lower part of the back radiating to the lower limbs and visual hallucinations appeared.

Neurologic Examination.—There were flexion and extension movements in the left lower extremity, right foot drop and weakness of the muscles of the lower extremities, more marked on the right side. The deep reflexes were hyperactive in the upper and depressed in the lower extremities. There were positive Mendel-Bechterew and Rossolimo responses on the right side. Hypesthesia, hypalgesia and thermohypesthesia were present from about the third lumbar to the first sacral segment. When the patient was pricked with a pin, he overreacted to the stimulus and complained of severe pain. Dragging of the pin produced the same reaction. A level was present at the fourth dorsal segment at which overreaction to pinprick was extreme. Cold was called hot below the fourth lumbar segment and in the perianal region. The sense of position was impaired in the fingers and toes, and sensibility to vibration was diminished in the lower extremities.

Autopsy.—The brain was normal.

The spinal cord was thin in the middle and lower portions of the thoracic region, and the crossed pyramidal tracts appeared translucent. Sections in the cervical region of the spinal cord disclosed demyelinization of the fasciculi graciles, crossed pyramidal tracts and cerebellar pathways, part of the anterior pyramidal tracts and the lateral and ventral spinothalamic tracts. The periphery of the spinal cord was more involved than the center (fig. 4). The tracts mentioned were more markedly involved in the thoracic and lumbar regions. The roots showed no pathologic changes. A minute histopathologic study, however, revealed a process seen in cases of toxic myelopathy.

Comment.—This is the only case of hyperpathia and subjective disturbances of sensibility to heat in our series of cases of toxic myelopathy. The pains were not those observed in cases of involvement of the posterior roots, and as the posterior roots did not disclose any pathologic changes, we are inclined to believe that the disturbances in

the present case were caused by the lesion in the spinothalamic pathways. Of interest in this case is the fact that the subjective disturbances of pain and temperature sensibility were associated with the impairment of these types of sensation.

CASE 5.—*Subacute combined degeneration of the cord with typical changes in the posterior and lateral columns and the level of the lesion at the sixth dorsal segment. "Spontaneous pain" and disagreeable sensations elicited by pinprick stimuli.*

History.—A. L., a woman aged 55, was admitted to the hospital on Aug. 30, 1929, with a history typical of cases of pernicious anemia and subacute combined degeneration of the spinal cord and with complaints of disagreeable pains in the lower extremities.

Neurologic Examination.—Weakness of the muscles of the lower extremities, bilateral signs of involvement of the pyramidal tract, depressed ankle jerks and a type of ataxia in the upper limbs referable to the posterior columns were observed. Hypesthesia and hypalgesia were observed below the sixth dorsal dermatome. The sense of position was impaired in the toes and fingers.

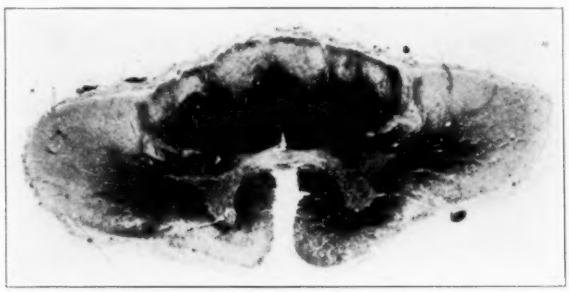

Fig. 4 (case 4).—Section from the cervical region showing demyelinization of the pathways at the periphery of the spinal cord. The spinothalamic tracts were also partly involved. Myelin sheath stain.

Vibratory sensation was lost at and below the hips and was impaired in the fingers. Pinprick stimuli below the sixth dorsal segment produced a disagreeable sensation and also severe pain. Squeezing of the muscles, deep pressure and rubbing of skin below the same level were disagreeable. Heat and cold were recognized below the level; but errors were frequently made, and cold produced at times a disagreeable sensation of pain.

Autopsy.—Transverse sections of the spinal cord at various levels disclosed demyelinization of the posterior columns and pyramidal pathways. In addition to that, from the sixth to the eighth dorsal segment practically all the fiber tracts, including the spinothalamic tracts, were partly destroyed (fig. 5). Furthermore, the spinal cord was distorted, and only the pyramidal tracts were spared slightly. The posterior roots were not involved.

Comment.—This patient, who suffered from subacute combined degeneration of the spinal cord had, in addition to the neurologic signs and symptoms typical of this disease, a transverse lesion at the sixth

dorsal segment with involvement of the spinothalamic pathways. Of interest was the fact that all modalities of sensation were impaired below the sixth dorsal dermatome. As in our other cases, various stimuli induced painful and disagreeable sensations.

LESIONS AT THE BULBAR LEVEL

The type of subjective sensory disturbance resulting from implication of the spinothalamic tracts which has been described in our cases of disease of the spinal cord may also be encountered in cases of pathologic processes in the medulla oblongata, pons and mesencephalon.

Diseases of the medulla oblongata causing subjective sensory dis-

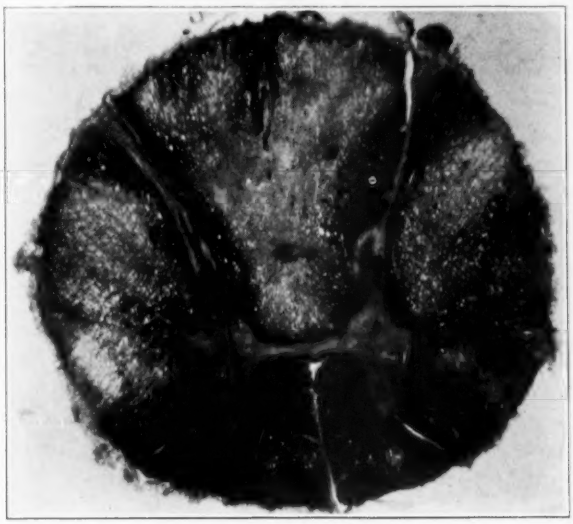

Fig. 5 (case 5).—Demyelinization of practically all the fiber tracts in the thoracic region in a case of subacute combined degeneration. Notice the partial implication of the spinothalamic tracts. Myelin sheath stain.

turbances are numerous. The close proximity of the spinal root of the trigeminal nerve and its nucleus to the spinothalamic tract at this level accounts for the objective and subjective sensory disturbances in the face on the side of the lesion and on the opposite side in the body. This condition is frequently encountered in cases of lesions of the posterior inferior cerebellar artery. A review of four cases of thrombosis of the posterior inferior cerebellar artery in which autopsy was performed did not disclose the phenomena associated with hyperpathia. Cases of this type in which necropsy was performed have been

described, however, by Senator,[15] Wallenberg,[16] Thomas [17] and Hun.[18] Foix, Thévenard and Nicolesco [19] recorded a case of paroxysmal excruciating pain in the distribution of the right and left trigeminal nerves. Operation did not relieve the pain. At necropsy the authors observed two small cavities within the nuclei of the descending roots of the trigeminal nerves on either side of the medulla oblongata. There have also been numerous clinical reports, but as the exact diagnosis can always be questioned, they are not cited here. Because he observed subjective sensory disturbances in a patient with thrombosis of the posterior inferior cerebellar artery, Wilson [14] was inclined to believe that there is a definite interrelation in some cases between spontaneous dysesthesias and a vascular (vasomotor, neurosympathetic) disorder. Such subjective sensory disturbances, as Wilson pointed out, were recorded as early as 1811 by Alexander Marcet [20] in a case of thrombosis of the posterior inferior cerebellar artery.

Pontile lesions causing subjective sensory disturbances are rarer. Weisenburg and Stack [21] were able to find only two clinical and two pathologic cases reported in the literature. The cases in which necropsy was performed were those of von Economo,[22] Mills [23] and Weisenburg and Stack. Mills' case was one of occlusion of the left superior cerebellar artery. In a series of nine cases of thrombosis of the superior cerebellar artery described by one of us (Davison [24]) and in other cases of inflammatory and neoplastic lesions, we observed sub-

15. Senator, H.: Apoplectische Bulbarparalyse mit wechselständiger Empfindungslähmung, Arch. f. Psychiat. **11**:713, 1881; **14**:648, 1883.

16. Wallenberg, A.: Anatomischer Befund in einem als Bulbaraffection (Embolie der Art cerebellar. post. inf.) beschriebenen Falle, Arch. f. Psychiat. **27**:504, 1895; **34**:923, 1901.

17. Thomas, H. M.: Symptoms Following the Occlusion of the Posterior Inferior Cerebellar Artery, J. Nerv. & Ment. Dis. **34**:48, 1907.

18. Hun, H.: Analgesia, Thermic Anesthesia and Ataxia, New York M. J. **1**:513, 1897.

19. Foix, C.; Thévenard, A., and Nicolesco, I.: Algie faciale d'origine bulbo-trigéminale au cours de la syringomyélie; troubles sympathiques concomitants; douleur à type cellulaire, Rev. neurol. **20**:900, 1922.

20. Marcet, Alexander: History of a Singular Nervous or Paralytic Affection Attended with Anomalous Morbid Sensations, Med.-Chir. Tr., London **2**:217, 1811.

21. Weisenburg, T. H., and Stack, S. S.: Central Pain from Lesions of the Pons, Arch. Neurol. & Psychiat. **10**:500, 1923.

22. von Economo, C.: Ueber dissoziierte Empfindungslähmung bei Ponstumoren und über die zentralen Bahnen des sensiblen Trigeminus, Jahrb. f. Psychiat. u. Neurol. **32**:109, 1911.

23. Mills, Charles K., in discussion on Weisenburg and Stack.[21]

24. Davison, C.; Goodhart, S. P., and Savitsky, N.: The Syndrome of the Superior Cerebellar Artery and Its Branches, Arch. Neurol. & Psychiat. **33**:1143 (June) 1935.

jective sensory disturbances in one case. In Weisenburg and Stack's case marked impairment of deep sensibility and lesser disturbance of superficial sensibility were accompanied by hyperaffectivity. In von Economo's case a hyperaffective state was observed in the presence of a total loss of superficial sensation. In both of these cases the spinothalamic tracts were implicated to some degree by tuberculoma of the pons. Weisenburg and Stack expressed the belief that for "central pain" to be perceived some of the fibers of the spinothalamic tract must be intact. We found no reports of cases in the literature in which lesions of the mesencephalon produced subjective sensory disturbances.

LESIONS AT THE THALAMIC LEVEL

When "spontaneous pain" and hyperaffective states were first described by Dejerine and later elaborated on by Roussy, it was generally accepted by them that this type of sensation can occur only in cases of pure thalamic lesions. Subsequent authors (Head and Holmes) have also expressed this opinion. Most observers have attributed the "spontaneous pain" to disease of the external nucleus of the thalamus, especially the posterolateral part. As already pointed out, Roussy formulated the *syndrome thalamique*, characterized by "spontaneous pain," hemianesthesia associated with loss of deep sensibility, astereognosis, little or no hemiplegia, hemiataxia and choreoathetoid movements. Since the publication of this valuable contribution numerous other cases have been recorded. Head, Holmes and others have established the fact that the "spontaneous pain," which is the essential part of the picture, may or may not be accompanied by the other symptoms. The most inconstant symptoms are the ataxia and choreo-athetosis.

Most of the cases so far described have occurred in cases of vascular lesions of the thalamus. The onset of the symptoms is sudden. The sensory disturbances consist of a profound impairment of deep sensibility and mild disturbances in superficial sensation. The "spontaneous pain" or other disagreeable subjective sensory disturbances may appear at the onset of the vascular lesion, soon after or much later. These usually last as long as the patient lives or may disappear at any period. As already emphasized by others, the pain may be constant or paroxysmal and is at times poorly localized and agonizing. It can be elicited by any type of stimulus, such as pinprick, touch or the application of heat and cold. Even the moving of certain objects in the room or the bed of the patient, noises, music and combing of the hair may induce severe pain. In addition to the "spontaneous pain" the patient may complain of other disagreeable sensations, such as burning, tingling, pricking, coldness and wetness.

Besides the cases described by Dejerine, Roussy and Holmes and Head,[25] other clinicopathologic cases have been recorded by Edinger,[26] Greiff,[27] Anton,[28] Muratow,[29] Long,[30] Winkler and van London,[31] Bonhoeffer,[32] Lewandowsky and Stadelmann,[33] Lhermitte,[34] Baudoin, Lhermitte and Lereboullet [35] and Hoffman.[36]

In cases 1 and 3 of Roussy's series there was destruction of the posterior part of the lateral nucleus of the thalamus throughout its entire extent and also of the posterior part of the internal capsule. In the cases described by Edinger, Winkler and van London and Holmes and Head the lesions were limited to the thalamus. Though most of the patients had "spontaneous pain," few had ataxia and choreo-athetosis. Choreo-athetosis occurred in about five of the recorded cases, in two of Roussy's cases and in the cases of Edinger, Greiff and Hoffman.

There were four patients with thalamic lesions and hyperaffective responses in our series.

CASE 6.—*Thrombosis of a branch of the right anterior choroidal artery with softening of the posterolateral surface of the external nucleus of the right thalamus. "Spontaneous pain" on the left side of the body, mild hemiplegia, hemiataxia and slight impairment of the superficial forms of sensation, with complete sparing of the deeper forms of sensibility.*

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25. Holmes, G., and Head, H.: A Case of Lesion of the Optic Thalamus with Autopsy, Brain **34**:255, 1911-1912.

26. Edinger, L.: Gibt es zentral entstehende Schmerzen? Deutsche Ztschr. f. Nervenh. **1**:262, 1891.

27. Greiff, F.: Zur Localisation der Hemichorea, Arch. f. Psychiat. **14**:598, 1883.

28. Anton, G.: Ueber die Beteiligung der grossen basalen Gehirnganglien bei Bewegungsstörungen und insbesondere bei Chorea, Jahrb. f. Psychiat. **14**:141, 1896.

29. Muratow, W. A.: Beitrag zur Pathologie der Zwangsbewegungen bei zerebralen Herderkrankungen,Monatschr. f. Psychiat. u. Neurol. **23**:510, 1908.

30. Long, E.: Deux observations anatomo-cliniques de syndrome thalamique, Rev. neurol. **19**:197, 1910.

31. Winkler, C., and van London, D. M.: About the Function of the Ventral Group of Nuclei in the Thalamus Opticus in Man, K. Akad. v. Wetensch. te Amsterdam, Proc. Sect. Sc. **2**:295, 1908-1909.

32. Bonhoeffer, K.: Klinisch-anatomische Beiträge zur Pathologie des Sehhügels und der Regio subthalamica, Monatschr. f. Psychiat. u. Neurol. **67**:253, 1928.

33. Lewandowsky, M., and Stadelmann, E.: Chorea apoplectica, Ztschr. f. d. ges. Neurol. u. Psychiat. **12**:530, 1912.

34. Lhermitte, J.: Les syndromes thalamiques dissociés; les formes analgiques et hémialgiques, Ann. de méd. **17**:488, 1925.

35. Baudoin, A.; Lhermitte, J., and Lereboullet, J.: Une observation anatomo-clinique d'hémorragie du thalamus, Rev. neurol. **2**:102, 1930.

36. Hoffman, W.: Thalamussyndrom auf Grund einer kleinen Läsion, J. f. Psychol. u. Neurol. **45**:362, 1933.

History.—M. B., a woman aged 56, was admitted to the hospital on May 1, 1923, with a history of severe pain in the left lower extremity and occasional pains in the left shoulder since 1922. The pains in the leg were said to be due to sciatica. At this time a diagnosis of auricular fibrillation was made. In August 1922 she awoke one morning with weakness of the entire left side associated with cramplike, spontaneous, sticking pains and numbness. The pains were aggravated by movement.

Physical Examination.—The heart was enlarged, with auricular fibrillation and mitral stenosis and insufficiency.

Neurologic Examination.—Mild left hemiparesis and hyperreflexia were noted but no Babinski response. There were coarse tremors in the finger-to-nose test and ataxia on the left side. Pinprick, temperature and touch sensibility on the left side were slightly impaired. The dragging of a pin was annoying on the entire left side of the body and felt like the rubbing of a rough turkish towel. Pinprick was very disagreeable and gave rise to pain. Applications of cotton-wool were experienced as the rubbing of sandpaper. The stimuli were perceived as uncomfortable and diffuse radiating sensations. Vibration evoked similar disagreeable affects. There were no disturbances of deep sensibility. Astereognosis was not present.

Course.—In 1930 it was noted that loud jazzy music aggravated the spontaneous pains on the left side, as did also loud noises and crying. Combing the hair was also disagreeable on the left side. The pains were so severe that morphine was resorted to early in the course of the illness, and ultimately the patient received as much as 2½ grains (0.16 Gm.) daily, frequently without any relief from the pain. In February 1932 she had another cerebrovascular insult, which was manifested by a period of confusion, dysarthric speech and twitching of the right corner of the mouth. The spontaneous pains remained unchanged. On Sept. 27, 1933, a speech disorder associated with weakness in the right upper extremity reappeared. The patient died of bronchopneumonia on Oct. 4, 1933.

Autopsy.—The brain was small, and the vessels at the base contained a few atheromatous plaques, most noticeable in the basilar artery. The brain was cut coronally, and areas of softening were observed in the course of the left lenticulostriate and the right anterior choroidal artery.

Coronal sections through the anterior part of the thalami revealed an area of softening on the left side involving the internal capsule and the putamen. This area of softening was most pronounced on the outer surface of the putamen and extended into the external capsule and claustrum. Sections passing through the other thalamic nuclei, slightly anterior to the mamillary bodies, showed the same process as described in the previous sections. The lateral ventricles were slightly dilated, and the left hemisphere appeared to be slightly smaller than the right. In a section through the mamillary bodies, besides the area of softening previously mentioned, there was also a small area of softening in the external nucleus of the right thalamus impinging on the internal capsule and slightly on the fasciculus thalamicus (fig. 6 *B*). Part of the lamina medullaris externa was destroyed by it. The other nuclear masses of the thalamus, the corpus Luysi, the substantia nigra, the cerebral peduncle and the anterior part of the mamillary bodies were not involved. In a section through the posterior surface of the mamillary bodies and the corpora Luysi, in addition to the lesion on the left side already described, there was also a small lesion of the external nucleus of the thalamus destroying the structures that have been enumerated and involving slightly the fasciculus thalamicus and the zona incerta (fig. 6 *C*). In certain regions the area of soften-

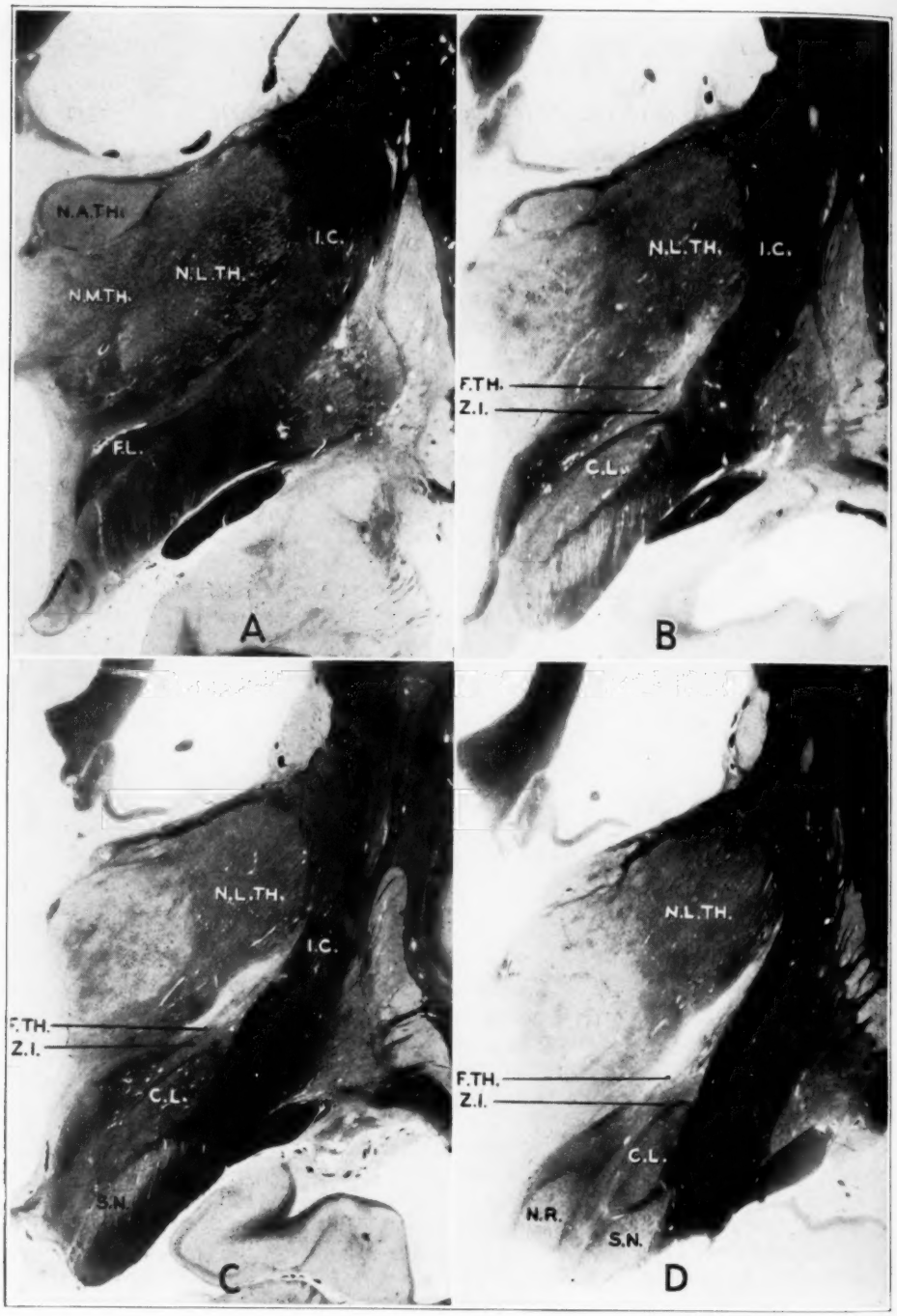

Fig. 6 (case 6).—*A*, coronal section through the thalamic nuclei barely showing the beginning of the area of softening in the inferolateral part of the lateral nucleus of the right thalamus. *B*, coronal section through the thalamic nuclei and corpus Luysi. The area of softening in the right lateral nucleus of the thalamus partly destroyed the lamina medullaris externa and impinged slightly on the internal capsule and fasciculus thalamicus. *C*, coronal section through the posterior part of the mamillary bodies and corpus Luysi. The area of softening destroyed part of the inferolateral part of the right external nucleus of the thalamus, the lamina medullaris externa, part of the fasciculus thalamicus and the zona incerta. *D*, coronal section through the corpus Luysi and beginning of the red nucleus. The area of softening destroyed part of the lateral nucleus of the thalamus, lamina medullaris externa, fasciculus thalamicus and zona incerta. In this figure and in figure 7, *N.A.TH.* indicates nucleus anterior thalami; *N.M.TH.*, nucleus medialis thalami; *N.L.TH.*, nucleus lateralis thalami; *I.C.*, capsula interna; *F.L.*, fasciculus lenticularis; *F.T.H.*, fasciculus thalamicus; *Z.I.*, zona incerta; *C.L.*, corpus Luysi; *N.R.*, nucleus ruber; *S.N.*, substantia nigra, and *PUL.*, pulvinar. Myelin sheath stain.

ing lay between the lamina medullaris externa and the zona incerta. In a section through the beginning of the red nuclei the lesion in the lateral nucleus of the right thalamus involved practically the same structures (fig. 6*D*). In a section through the pulvinar the lesion could no longer be visualized (fig. 7). Secondary degeneration was present in the radiating fibers of the external nucleus of the thalamus, in the external medullary lamina of the thalamus and in some of the fibers of the internal capsule. There was nothing of note in the pons. The medulla oblongata revealed only slight hypertrophy of the left olive. In cresyl violet preparations the areas of softening in the left putamen and in the right thalamus consisted of numerous compound granular corpuscles, broken-down myelin

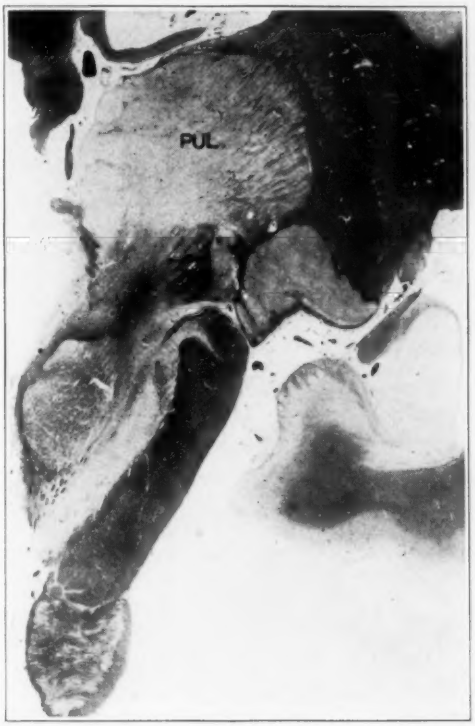

Fig. 7 (case 6).—Coronal section through the pulvinar and red nucleus. The area of softening at this level can no longer be visualized. Myelin sheath stain.

and slightly proliferated and thickened vessels. The ganglion cells of the external nucleus of the right thalamus bordering this area of softening showed pigmentary atrophy. Numerous ganglion cells of the external nucleus of the thalamus within the area of softening had undergone various pathologic changes.

Sections of the spinal cord disclosed descending demyelinization of the right crossed pyramidal tract.

Comment.—The outstanding clinical features in this case were the "spontaneous pains" in the left side of the body, mild hemiplegia, hemiataxia, slight impairment of superficial forms of sensation and

complete sparing of the deeper forms of sensibility. The "spontaneous pains" were present for eleven years. The lesion, a very small one, extended through the posterior part of the external nucleus of the right thalamus along its inferolateral border, destroying the lamina medullaris externa and impinging on the internal capsule and the fasciculus thalamicus (figs. 6 and 7). It lay between the lamina medullaris externa and the zona incerta.

In contrast to the classic cases described in the literature by Roussy, and Holmes and Head, the deeper forms of sensibility, which are generally involved, were spared completely in our case, while the more superficial types of sensation were slightly implicated. In Edinger's case the sense of position was unaffected, and the only disturbance recorded, in addition to the hyperaffective responses to certain stimuli, was a slight diminution of temperature sense. Bonhoeffer expressed the belief that disturbances of temperature sensation are due to lesions in the posterior part of the lateral nucleus of the thalamus. Cases in which the "spontaneous pains" are not accompanied by disturbances in deep sensibility were also described by Hillemand [37] and by Lhermitte. Choreo-athetosis was absent in our case. The location and extent of the lesion in this case conforms more with those in the case reported by Hoffman. In the other cases recorded in the literature more extensive lesions were shown.

Of interest in our case is the fact that loud jazzy music and also noises and crying aggravated the "spontaneous pains." In this respect it resembles the cases described by Head and Holmes in which music or disagreeable sounds affected the pains.

CASE 7.—*Neoplasm in the left frontoparietal region compressing the thalamic nuclei. Signs and symptoms of a neoplasm in the frontoparietal region, flaccid hemiplegia, hyperaffectivity and hemisensory disturbances.*

History.—I. H., a man aged 28, who was admitted to the hospital on Jan. 21, 1932, fainted while at work in July 1931 and fell, striking the region of the left frontal lobe. He returned to work in a week and thereafter complained of nocturnal headaches. He became weak and was confined to bed. On Nov. 11, 1931, he was operated on, and an astrocytomatous cyst was partially removed from the left frontal lobe. Two weeks after operation he became worse, and the brain was reexplored. A week later sudden hemiplegia and aphasia appeared.

Neurologic Examination.—Flaccid right hemiplegia with signs of involvement of the pyramidal tracts, partial aphasia, right homonymous hemianopia and paralysis of the lower two thirds of the face were present. The right hand was warmer than the left. Touch, pain and temperature senses were impaired on the right side. Cold applications produced a disagreeable sensation of pain. Sensation for vibration was diminished on the right side. The senses of position, point discrimination and stereognosis could not be tested. There was bilateral papilledema. The pupils were dilated and reacted poorly to light and in accommodation.

37. Hillemand, P.: Contribution à l'étude des syndrômes de la region thalamique, Paris, Jouve & Cie, 1925.

Course.—On Aug. 5, 1932, one of us detected marked hypersensitivity to tactile stimulation on the entire right side of the body. The patient could not stand having the examiner's hand touch any part of the right side. He was too ill for a careful study to be made at that time. Toward the end of his stay jacksonian convulsions and then meningitis and pneumonia developed. He died on Aug. 9, 1932.

Autopsy.—There was a large tumor of the left hemisphere, which extended from the frontal to the parietal region and destroyed most of the frontal, orbital, precentral, postcentral and temporal convolutions. Coronal sections disclosed destruction of the diencephalon. Sections through the thalamic nuclei stained for myelin sheaths showed destruction of the parietal and temporal convolutions and also compression with almost complete destruction of the nuclei of the left thalamus, especially the lateral nucleus (fig. 8). The medial nucleus was somewhat spared.

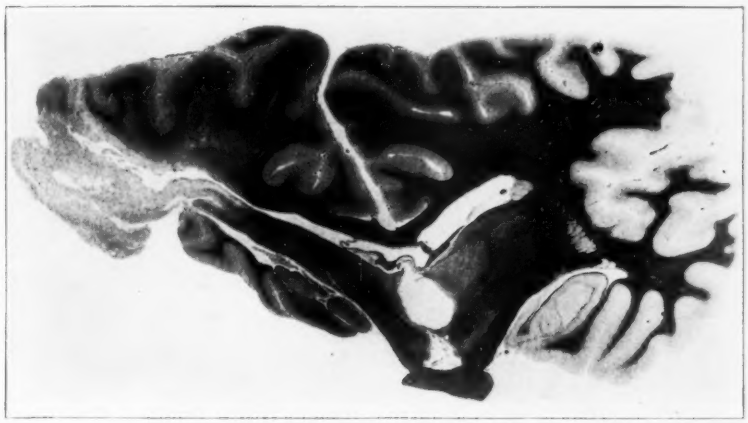

Fig. 8 (case 7).—Coronal section through the thalamic nuclei showing distortion of the thalamic nuclei on the left side, especially the lateral nucleus. Notice the destruction of the left parietal and temporal convolutions. Myelin sheath stain.

Comment.—This patient, in addition to symptoms and signs of a frontoparietal neoplasm, presented signs of flaccid right hemiplegia, disturbances of superficial sensation on the right side and hyperaffectivity. Deep forms of sensation, except vibration, could not be tested adequately. As shown in the preparations, the nuclei of the left thalamus were destroyed and compressed by the neoplasm, the lateral nucleus being most, and the medial and anterior nuclei least, involved. In view of the fact that the external nucleus of the thalamus was compressed, we are inclined to attribute the disagreeable painful sensation to the implication of this structure instead of to disease of the parietal convolutions. The latter possibility cannot be totally excluded.

CASE 8.—*Neoplasm in the left parieto-occipital region with invasion of the pulvinar. Overreaction to pain; impairment of superficial forms of sensation.*

History.—M. V., a woman aged 39, was admitted to the hospital on Jan. 5, 1933, with a history of headaches of ten years' duration. In June 1932 visual impairment and defective memory were noted. In July 1932 she entered the Neurological Institute, where a diagnosis of tumor of the occipital lobe was made. An operation was performed on Aug. 4, 1932, and a glioblastoma multiforme was partially removed from the left occipital lobe. A second operation was performed without a great deal of benefit.

Neurologic Examination.—Right hemiparesis, signs of involvement of the pyramidal tracts on the right side, weakness of the right lower portion of the face on volitional and emotional innervation, right homonymous hemianopia, sensory aphasia and mental defect were noted. Pain, touch and temperature senses were impaired on the right side. There was overreaction to pinprick in the right arm. The mental condition did not permit the making of satisfactory sensory studies. Bilateral papilledema and weakness of the left external rectus muscle were noted.

Autopsy.—A neoplasm was situated in the left parieto-occipital region, destroying most of the convolutions. When the brain was cut coronally, the white matter of the left hemisphere as far as the precentral region was observed to be edematous. Sections through the thalamic nuclei stained by the myelin sheath method disclosed pallor for all the white fibers due to edema (fig. 9 *A*). The external and other thalamic nuclei at that level were intact, except that the fibers of the external medullary lamina of the external nucleus of the left thalamus stained less well than the corresponding fibers on the right side (fig. 9 *A*). The neoplasm did not invade the thalamic nuclei at that level. In a section through the pulvinars the tumor was seen to have destroyed the following structures on the left side: the greater part of the pulvinar, part of the white fibers of the convolutions of the island of Reil, the centrum ovale and the corpus callosum (fig. 9 *B*).

Comment.—There was impairment of superficial sensation, with overreaction to pain. The sensory status could not be investigated satisfactorily because of the patient's mental condition. The tumor, in addition to its implication of the parieto-occipital convolutions on the left side destroyed the greater part of the pulvinar. The external nucleus of the left thalamus, however, remained intact. Pressure on it due to edema may be considered as a possible cause of the "central pain." In view of the fact that the parietal convolutions also were implicated, it is difficult to establish the rôle they may have played in the overreaction to pain and in the impairment of superficial sensation. In some of the cases of thalamic involvement recorded by Roussy, Holmes and others, lesions of the pulvinar were observed.

This case is of interest because of Hillemand's attempt to classify the thalamic syndrome as pure and typical forms and formes frustes. In the pure forms the lesion is in the thalamus only and is caused by closure or disease of the rami of the thalamogeniculate arteries. The pure forms are the same as those described by Dejerine, Roussy and others. In typical forms there is also obliteration of the posterior cerebral artery. In addition to the symptoms cited, hemianopia, and in cases of lesions of the left side, alexia also are present. In the

formes frustes the hyperaffectivity is not associated with objective sensory phenomena. There may be hemianopia and slight chorea. Although the lesion in this case was neoplastic, the added symptom of hemianopia places it in Hillemand's second group. It should be

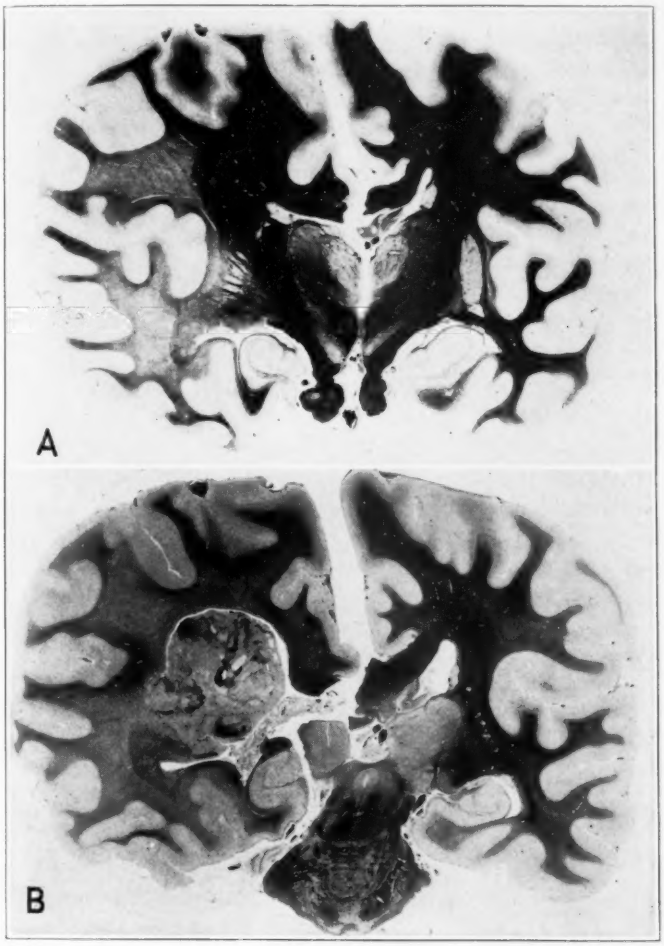

Fig. 9 (case 8).—*A*, coronal section through the thalamic nuclei showing edema of the left hemisphere. The thalamic nuclei appear intact and the lamina medullaris externa stained poorly. *B*, coronal section through the pulvinars showing destruction of the left pulvinar as well as of the white fibers of the insular convolutions and centrum ovale. Myelin sheath stain.

emphasized that ataxia and choreo-athetoid movements were absent. Ataxia may have been present, but it could not be elicited because of the patient's mental condition.

CASE 9.—*Multiple cerebral aneurysms. Partial involvement of the thalamic nuclei on the left side. Hyperpathia and impairment of superficial sensation. Because of the aphasia the deeper forms of sensation could not be tested.*

History.—M. H., a woman aged 38, was admitted to the hospital on Aug. 6, 1929, with a history of the appearance of generalized convulsions in 1917. They recurred until March 1929, when paralysis of the right side and aphasia suddenly developed.

Neurologic Examination.—Right spastic hemiplegia with evidences of apraxia, motor and sensory aphasia and right homonymous hemianopia and hypesthesia, hypalgesia and thermohypesthesia on the right side were noted. The deeper forms of sensibility could not be tested satisfactorily because of the aphasia. Attempts to manipulate the right side of the body produced such intense pain that the patient shrieked, and any stimuli applied to the right side of the body caused severe pain. The patient died on Dec. 13, 1932, following a convulsive seizure.

Autopsy.—Multiple aneurysms were observed throughout the central nervous system, the larger ones being located in the left hemisphere. There was a large cystic area in the region of the second and third frontal, precentral, postcentral and insular convolutions on the left side. The external and internal capsule and the claustrum, striatum, pallidum and thalamic nuclei, including the external nucleus, on the left side were also partially destroyed (fig. 10).

Comment.—This patient had definite hyperpathia and impairment of superficial sensation. The modalities of deep sensation could not be tested satisfactorily because the patient was aphasic. We are inclined to attribute the hyperaffectivity to the lesion in the external nucleus of the left thalamus. It should be admitted that the lesions in the left parietal lobe cannot be ruled out as a causative factor, because such lesions may cause hyperpathia. Our next two cases will illustrate this point. In cases in which both the external nucleus of the thalamus and the parietal convolutions were implicated, we were inclined to consider the "spontaneous pain" as being due to the lesion in the thalamus. In cases of pure lesions of the parietal lobe, however, we were forced to consider spontaneous pain and other subjective sensory disturbances to be of cortical origin. The right homonymous hemianopia in this case was due to a separate aneurysm of the occipital lobe and therefore does not place the case in the same group as case 8.

LESIONS AT THE CORTICAL LEVEL

"Spontaneous pain," "central pain" and other subjective and objective types of sensory disturbance concerned with pain and temperature observed at various levels in the course of the spinothalamic pathways, according to Head and Holmes, are not encountered in cases of pure lesions of the cortex. According to Head and Holmes, the "optic thalamus is the center of consciousness for certain elements of sensation, or the thalamus is the seat of the physiological processes which underlie crude sensation of contact, heat and cold, together with the feeling tone they evoke." Head and Holmes have expressed the opinion

that pain and thermal sensations are least affected by pure cortical lesions and tactile sensation more so. Holmes stated that in order to test Head's conclusions the disease in the selected cases must be limited to the cerebral cortex and must be of "such duration that the effects of shock and other indirect disturbances due to the lesion have passed off." Another factor which must be eliminated is the presence of hysterical phenomena, observed occasionally in cases of cerebral lesions, especially the so-called hysterical anesthesia observed by Holmes in cases of gunshot wounds and vascular and other lesions of the brain.

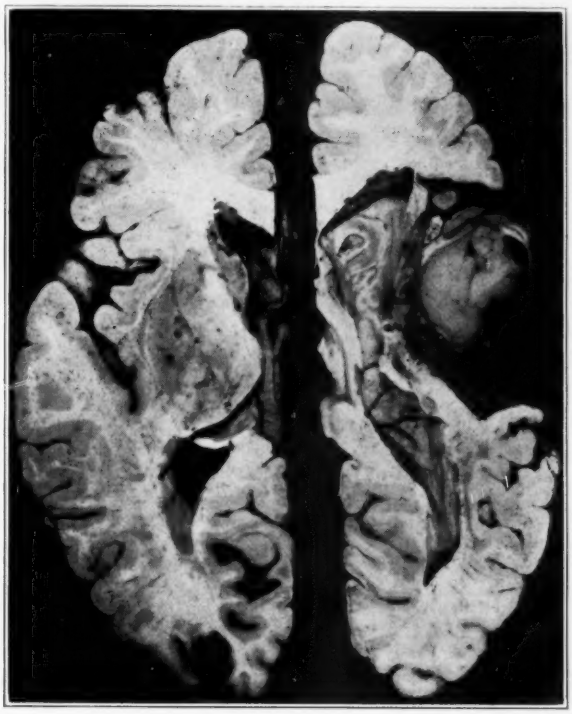

Fig. 10 (case 9).—Aneurysm of the left hemisphere destroying and compressing the thalamic nuclei. Notice the destruction of the insular and other convolutions.

A number of other observers have maintained that subjective and objective painful and thermal sensations occur in cases of traumatic, vascular, neoplastic and other types of lesions of the cerebral cortex. Mills, as early as 1891, reported a case of bilateral meningitis of the convexity with softening of both the cortex and the subcortex of the parietal lobe of each side. In that case the analgesia was complete and was variously distributed over both sides of the body. Mills concluded that common sensibility, including that to pain, touch and temperature, is

represented bilaterally in the cortex. He agreed, however, with Head and Holmes that the function of the sensory cortex is largely one of discrimination. Later Piéron, Foerster, Marie and Bouttier, Goldstein,[38] S. A. K. Wilson, Guillain and Bertrand [39] and others recorded cases of cortical lesions in which there were either subjective or objective sensory disturbances of pain and temperature sensibilities. Goldstein admitted that pain is cortically represented, although not as extensively as the other forms of sensation. He localized cutaneous sensation in the anterior part of the postcentral gyrus. Marie and Bouttier also emphasized that the cortex is concerned with the perception of pain. Cushing [40] observed in two patients that when the postcentral gyrus was stimulated, one patient experienced a sensation of numbness, while the other perceived a tactile sensation; pain was not elicited in either case. Foerster observed in a patient with jacksonian epilepsy that the aura invariably consisted of pains in the bladder and rectum followed by paresthesia on one side. He expressed the belief that the pain was of cortical origin. In addition, he succeeded in producing painful and disagreeable sensations in one half of the body by electrical stimulation of the postcentral and superior parietal convolutions of the opposite side. S. A. K. Wilson described a case of jacksonian epilepsy in which thermal dysesthesia constituted an aura due to cortical involvement. As autopsy was not performed, it is possible that other neural structures besides the cortex may have been involved. Parker [41] recorded a case of tumor of the brain in which the sensory portion of the cortex and subcortical white matter on the left side were involved, with apparent sparing of the optic thalamus. The patient had "spontaneous pain" in the right arm and leg and right side of the face and made jerking movements. The onset of the jerking movements was accompanied by a burning, aching, pulling sensation of the face and right arm. The patient complained that the right arm felt hot and swollen. Sensory examination disclosed a mild impairment of sensation for pain, temperature and touch over the entire right side of the body. As the brain was not cut serially, it is difficult to state whether parts of the internal capsule and thalamus were not affected. The possibility that a tumor was compressing the external nucleus of the thalamus and internal capsule and acting as an irritating factor cannot be completely excluded. In that

38. Goldstein, K.: Die Topik der Grosshirnrinde in ihrer klinischen Bedeutung, Deutsche Ztschr. f. Nervenh. **77**:7, 1923.

39. Guillain, G., and Bertrand, I.: La nécrose atrophique symétrique des circonvolutions pariétales ascendantes et des convolutions occipitales, Ann. de méd. **31**:35, 1932.

40. Cushing, H.: A Note upon the Faradic Stimulation of the Postcentral Gyrus in Conscious Patients, Brain **32**:44, 1909.

41. Parker, H. L.: Pain of Central Origin, Am. J. M. Sc. **179**:241, 1930.

respect the case may resemble our cases 7, 8 and 9, which we classified as cases of thalamic lesions. In Guillain and Bertrand's case there were involuntary athetoid movements and intense pain in the left upper extremity. In addition, hypesthesia, hypalgesia and thermohypoesthesia, loss of position sense and two point discrimination and bilateral astereognosis were noted. At necropsy the thalami were observed to have been spared, but there were bilateral symmetrical softenings of the occipitoparietal regions, with partial involvement of the precentral region. In view of the bilaterality of the lesion, interpretation is difficult, but the pain may have been produced by the lesion in the right ascending parietal gyrus.

Dusser de Barenne [42] succeeded in producing hyperesthesia and hyperalgesia in animals by applying strychnine to some areas of the cortex in front of or behind the central sulcus. He concluded that both the precentral and the postcentral portions of the cortex are concerned in these sensory perceptions. Minkowski [43] from his animal experiments also concluded that the cortex is concerned with pain and thermal modalities of sensation.

Head and Holmes questioned the clinicopathologic cases and stated that the lesions were "probably not purely cortical, or were accompanied by disease of the internal capsule, thalamus or deeper parts of the brain; in others the effect of shock or of recent epileptiform attacks may have been present; or it may be that an unrecognized hysterical anesthesia complicated the organic picture; but it is probable that in many instances a mere subjective disturbance, unaccompanied by any alteration of the threshold, was interpreted as hypalgesia."

The two cases to be described, of cortical lesions with objective and subjective sensory disturbances, support the theory of cortical representation for pain and temperature sensation. In the first case, in which an adequate clinical and pathologic study was made, there was no question of superimposed capsular, thalamic or other deeper structural involvement to account for the sensory disturbances. We also believe that we have eliminated the possible confusing elements of shock, recent epileptiform convulsions, hysterical anesthesia and subjective disturbances unassociated with alteration of the threshold to painful stimuli and interpreted as hypalgesia.

CASE 10.—*Occlusion of the right postcentral and posterior parietal branches of the middle cerebral artery with destruction of the postcentral, superior parietal,*

42. Dusser de Barenne, J. G.: Experimental Researches on Sensory Localization in the Cerebral Cortex of the Monkey, Proc. Roy. Soc., London, s.B **96**:272, 1924.

43. Minkowski, M.: Etude sur la physiologie des circonvolutions rolandiques et pariétales, Schweiz. Arch. f. Neurol. u. Psychiat. **1**:389, 1917.

superior temporal and insular convolutions, the thalamic nuclei remaining intact. Flaccid left hemiplegia, involuntary movements of the left upper extremity, "spontaneous pain" and impairment of the superficial and deeper forms of sensation on the left side.

History.—A. A., a man aged 53, was admitted to the hospital on May 6, 1932, with a history of mitral stenosis and insufficiency of several years' duration. In April 1931 a cerebrovascular insult on the right side resulted in paresis and sensory disturbances on the left side and led to complaints of "spontaneous pains" and pain in response to light touch over the left side of the body. On eating or drinking warm or cold fluids the patient experienced sharp radiating pains over the left upper and lower extremities. When the hair over the left side of the head was combed, the same disagreeable sensation of pain was experienced.

Physical Examination.—There was evidence of long-standing rheumatic cardiac disease with mitral and aortic involvement, auricular fibrillation with a relatively slow ventricular rate and mild congestive heart failure. There was moderate peripheral arteriosclerosis with clubbing of the fingers.

Neurologic Examination.—There was flaccid left hemiparesis with diminished deep reflexes and absence of the achilles tendon jerk. Spontaneous spasmodic movements of various parts of the left upper extremity were noted. There were definite hypesthesia, hypalgesia and thermohypesthesia on the left side. Vibratory and stereognostic senses were impaired on the left side. Point discrimination could not be tested accurately. When the left side of the body was stimulated with cotton or pinprick or when any kind of pressure was applied to it, the patient experienced a disagreeable sensation, which he likened to the feeling of "irritating a sore." Pressure, movement and percussion were painful. Tests with the tuning fork produced similar sensations. The patient died of bronchopneumonia on Feb. 14, 1933.

Autopsy.—There was occlusion of the postcentral and posterior parietal branches of the right middle cerebral artery. There was an area of softening which destroyed the right insula and some of the parietal convolutions. The thalamic nuclei were intact. Serial sections through the destroyed convolutions and thalamus, stained by the myelin sheath method, disclosed destruction of the postcentral, superior parietal, superior temporal and insular convolutions (figs. 11 *A* and *B*). The claustrum and the external capsule on the right side were also destroyed. The internal capsule, the external nucleus of the thalamus and the other thalamic nuclei were intact (fig. 11 *A* and *B*). In a section through the atrium ventriculi (fig. 11 *C*) there was partial destruction of the superior and inferior parietal and superior temporal convolutions.

Comment.—The flaccid hemiplegia, the spontaneous spasmodic movements of various segments of the left upper extremity, the impairment of superficial and deep sensation on the left side and the hyperaffectivity strongly suggested a *syndrome thalamique* with a lesion in the external nucleus of the thalamus. Postmortem observation showed a lesion of the right postcentral and superior parietal convolutions without any implication of the external nucleus or other nuclei of the thalamus or of the internal capsule. The careful study of the serial sections in this case, we believe, proves that the parietal portion of the cortex is concerned with the appreciation of touch, pain and temperature

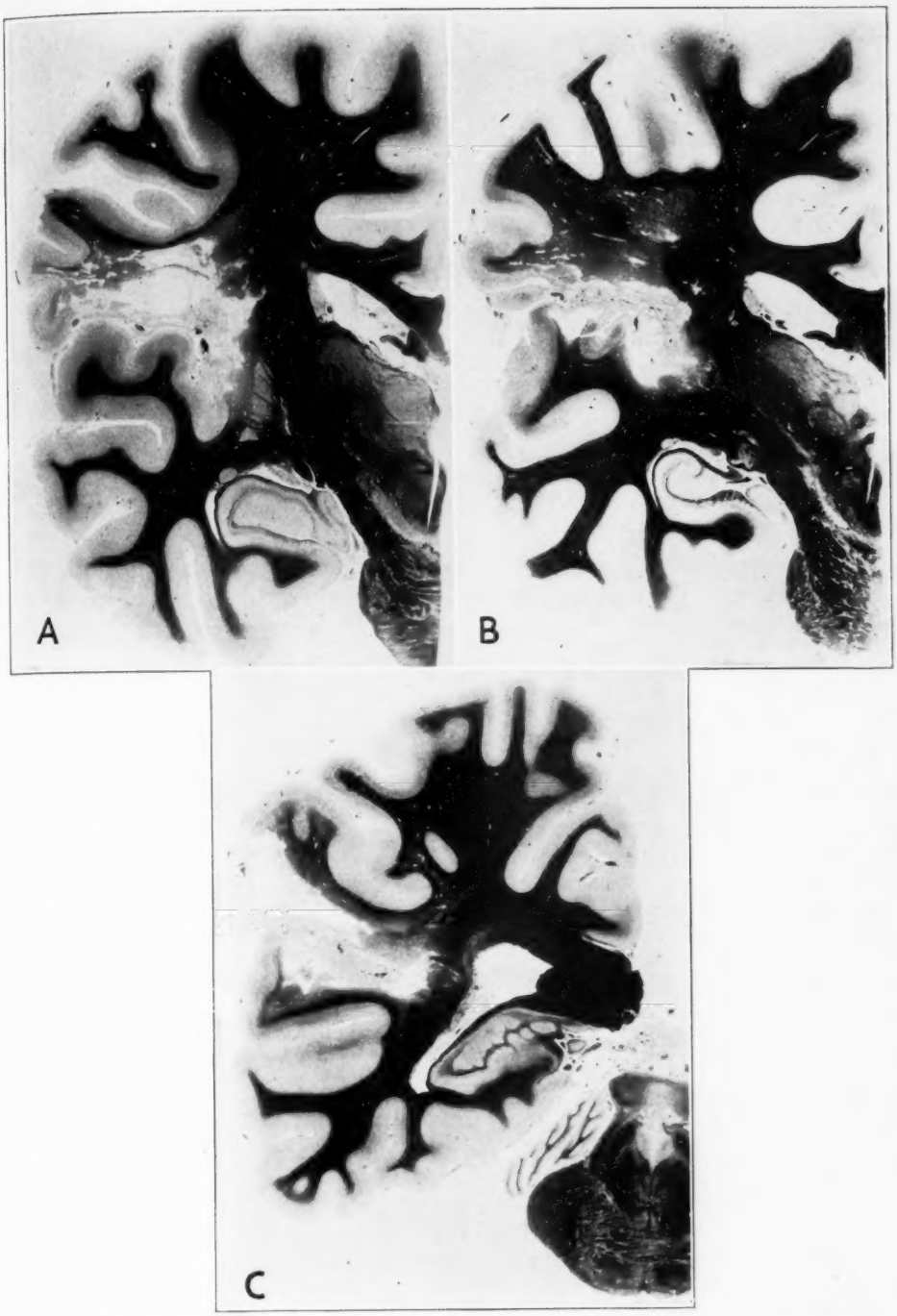

Fig. 11 (case 10).—*A*, coronal section through the thalamic nuclei showing an area of softening along the postcentral and posterior parietal branches of the right middle cerebral artery implicating the postcentral, insular and superior temporal convolutions. Notice the absence of thalamic involvement. *B*, section slightly below *A*, showing the absence of thalamic involvement. *C*, coronal section through the atrium ventriculi showing partial destruction of the parietal and superior temporal convolutions. Myelin sheath stain.

as well as with the causation of "spontaneous pain." This case was clearcut in that there were no other embolic or thrombotic lesions anywhere along the cerebrospinal axis.

In discussing the paper of Weisenburg and Stack on "central pain," Mills spoke of a case in which the "thalamic syndrome" was caused by a lesion above the thalamus, i. e., a neoplasm of the parietal lobe which spared the thalamus. Parker recorded a similar case. The factor of irritation or distant effect in cases of neoplasm might be brought up to refute the theory of cortical representation for such types of sensation. We are not aware that the literature records any cases in which there was such clearcut destruction of the parietal convolutions, with sparing of the internal capsule and thalamus and the presence of the types of subjective and objective sensory disturbances that are represented in our case. This case again brings up the question as to whether Mills, Piéron, Marie and Bouttier, Foerster and S. A. K. Wilson were not correct in the assumption that the cortex is concerned with painful and thermal modalities of sensation.

CASE 11.—*Emboli to branches of the right middle and the left posterior cerebral artery, with partial occlusion; destruction of the postcentral and superior parietal convolutions on the right side, with sparing of the thalamic nuclei. Flaccid left hemiplegia, hyperaffectivity to all stimuli on the left side, a feeling of "electricity" on pinprick and impairment of all modalities of sensation which could be tested.*

History.—C. R., a woman aged 40, was admitted to the hospital on July 16, 1929, with a history of precordial pains, orthopnea, palpitation and dizzy spells of three years' duration. A diagnosis of mitral stenosis and insufficiency and auricular fibrillation was made. While she was under observation, diabetes mellitus and hypertension also developed. In 1926 sudden blindness of the left eye appeared and was followed by optic atrophy due to embolism of the central retinal artery.

Physical Examination.—Marked cyanosis, mitral stenosis and insufficiency, an enlarged liver and edema of both lower extremities were noted.

Neurologic Examination.—The patient was slightly confused. There was flaccid left hemiplegia, with signs of involvement of the pyramidal tracts and weakness of the left side of the face. The left upper extremity was edematous. There were hypesthesia, hypalgesia and thermohypesthesia on the left side. There was hyperaffectivity on the left side to all stimuli. Pinprick on the left felt like "electricity." The sense of position could not be tested. Vibratory sense was preserved. There was astereognosis on the left side. The patient died of bronchopneumonia on Nov. 16, 1932.

Autopsy.—There was slight softening of the right postcentral convolution. The right middle cerebral and left posterior cerebral arteries were slightly occluded. Serial horizontal sections through the thalamus revealed partial destruction on the right side of the precentral and postcentral and part of the superior parietal, insular and superior temporal convolutions (fig. 12), but no lesions of the thalamus or internal capsule. The left claustrum was also implicated. Another incomplete area of softening was noted in the left hemisphere along the distribution of the posterior cerebral artery, implicating the fusiform, inferior temporal and occipital convolutions.

Comment.—In this case, although the lesion was not as clearcut as in case 10, there were flaccid hemiplegia, disturbances involving all the modalities of sensation that could be tested and hyperaffectivity. Pinprick felt like "electricity." Autopsy revealed that the lesion was incomplete but resembled the lesion in case 10 in that the postcentral and superior parietal convolutions were implicated without thalamic or capsular involvement. The incomplete occlusion of the opposite posterior cerebral artery did not affect the thalamus and could not have

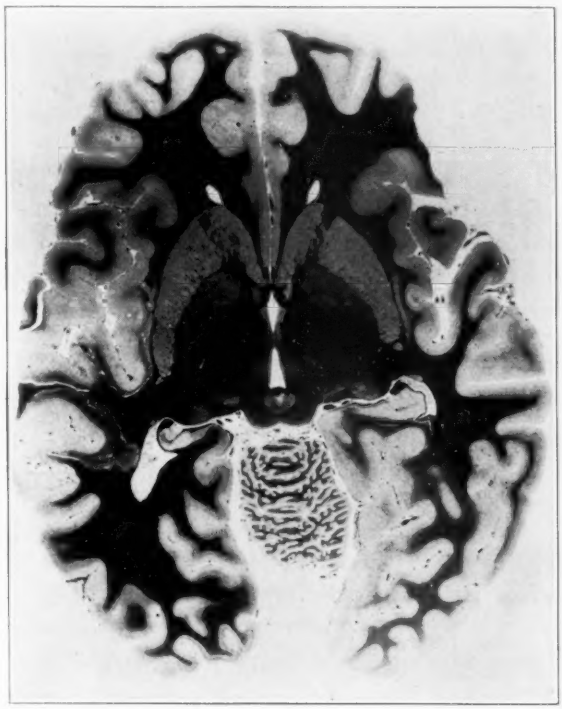

Fig. 12 (case 11).—Horizontal section through the diencephalon showing partial destruction of the left parietal, temporal and insular convolutions. The thalamic nuclei are spared. There is partial destruction of the convolutions along the distribution of the right posterior cerebral artery which could not have caused the sensory disturbances on the right side. Myelin sheath stain.

caused sensory disturbances on the same side. This case, like case 10, demonstrates that disturbances of sensation for pain and temperature can occur in cases of lesions of the parietal lobe.

PATHOPHYSIOLOGY

In early descriptions of the thalamic syndrome, Head and Holmes (1911) expressed the opinion that "central pain" is the product of

thalamic activity and that its control is "effected by means of paths from the cortex to the thalamus which probably end in its lateral nucleus." As "spontaneous pain" and other subjective sensory disturbances are conscious processes, it is reasonable to believe that afferent paths from the thalamus to the cortex conduct such stimuli and that the cortex must be intact in order for these stimuli to be perceived.

As pointed out in this paper, these subjective sensory disturbances were observed in cases of lesions other than those of the thalamus. In most of the lesions the spinothalamic tracts were implicated. It must be accepted at the outset that complete destruction of this pathway could not give rise to "central pain," for a tract which is at least not partly intact could not mediate these impulses. The necessity for integrity or partial integrity of these pathways for the appreciation of such impulses is accepted by most observers.

Head and Holmes explained the production of the subjective sensory disturbance on the theory of release. According to these authors the "central pain" is a release phenomenon that is rendered possible by removal of the inhibitory control which the cerebral cortex normally exerts on the thalamus, which is the main station concerned with the perception of pain. Against this is the argument of Wilson and others that if this theory for "central pain" is accepted, it must be accepted also for persistent thermal and other subjective sensory disturbances of central origin. If the theory of release is offered as the explanation of the presence of such types of sensation in cases of thalamic lesions, it should also be of value in the explanation of lesions found at lower levels, such as the pons, medulla and spinal cord. To support this conclusion sufficient evidence of the existence of cortical inhibitory pathways descending farther down than the thalamus would have to be presented, which thus far has not been done. For this reason S. A. K. Wilson and others have expressed the belief that the "irritation of the afferent sensory system—surely must appear as an at least equally feasible explanation, if not much more so."

Foerster attempted to explain "central pain" on the basis of the theory that there are two sensory systems: an affective sensory system for the appreciation of pain and of pleasant and unpleasant qualities in sensation and a pure sensory system concerned with touch, pressure, temperature discrimination and spatial appreciation, free from affective elements. The affective sensory system, according to Foerster, is regulated by the pure sensory system; and "central pain" is produced by a setting free of the affective system by the dysfunction of the pure sensory system which normally exercises control over it. The "central pain" observed in cases of bulbar lesions and lesions of the spinal cord he explained on the basis of lesions of the corticofugal inhibiting system,

which he said extends to these structures. He expressed the opinion that this pathway extends to the limiting layer in the lateral columns, close to the dorsal horn. When "central pain" occurs, the corticofugal inhibiting system no longer acts.

Many investigators of this subject, however, believe that the symptoms are the end-result of irritation of the sensory pathways, especially the spinothalamic tracts. Lewandowsky was of the opinion that "central pain" in cases of lesions of the spinal cord is usually caused by irritation of the posterior roots. He admitted that only in rare cases is "central pain" caused by irritation of the intramedullary tracts. The occurrence of "central pain," and frequently other associated sensory disturbances, on the side opposite the lesion in the spinal cord is conclusive evidence that the irritation in these cases is in the intramedullary tracts and not in the posterior roots.

This irritation can be produced by mechanical, chemical or electrical stimulation anywhere in the course of the spinothalamic tract, as is well substantiated by the cases that we have presented and by the records of other cases. Dusser de Barenne injected strychnine into the posterior horns of the cord, producing in this manner pain in the corresponding segmental cutaneous zones. Foerster observed that electrical stimulation of the anterior tracts also resulted in pain. These findings are additional corroborative evidence that lesions and irritation of the sensory pathways produce pain.

S. A. K. Wilson expressed the opinion that irritation of the sensory system and paths concerned is sufficient to explain the occurrence of spontaneous pain and the subjective sensory disturbances when these are not accompanied by objective sensory changes. He said that the sensory system is "partly irritated and partly under destruction" in the presence of objective sensory changes.

Because of the associated disease of the sympathetic nervous system or of the vascular system or of both in some cases of "central pain," Wilson concluded that "under certain circumstances a neural origin, and under others a vascular or sympathicovascular origin, underlies the manifestation in consciousness of tactile, painful, and thermal dysesthesiae." The proof he adduced for that theory is the fact that when blood vessels are ligated painful stimuli are produced. As further evidence he quoted Foerster's idea "of a continuous side path for vessel pain, constituted by afferent fibers which do not unite with nerve trunks but pass directly to the sympathetic paravertebral chain, eventually to enter the neuraxis at higher levels." Still more suggestive than that is the fact, mentioned by S. A. K. Wilson, of the disappearance of angiospasms and pain after periarterial sympathectomy and other operations on the arterial plexus.

The subjective sensation of wetness or "hygric dysesthesia," which is a dysesthetic compound of a tactile and a thermal element, Wilson explained as due to the possible "juxtaposition at peripheral or bulbar levels of touch and thermesthesia-conducting tracts."

Insufficient as these theories may be with regard to an explanation of the causation of "central pain," they are recorded here for their evaluation.

SUMMARY AND CONCLUSION

In this presentation an attempt has been made to show that "central pain" and other subjective sensory disturbances occur not only in cases of pure thalamic lesions but also in cases of peripheral, spinal cord, bulbar and cerebral lesions.

In our single case of lesion of a cranial nerve the subjective sensory disturbance consisted essentially of a burning sensation along the distribution of the trigeminal nerve. The neurofibroma compressing the nerve was undoubtedly the irritating factor for the production of that type of sensation.

In the four cases of lesions of the spinal cord, in addition to "central pain" there were other subjective sensory disturbances such as burning, "vibratory electric-like sensations" and distorted thermal sensations, i. e., cold being called hot. In most of the cases superficial sensation was impaired below the level of the lesion. The pain and temperature dysesthesias were associated with impairment of those forms of sensation. Histologic examination showed that the spinothalamic tracts were implicated. In the first case there was also slight involvement of the posterior columns in the region of the cervical enlargement. As in some of Holmes' cases, vibratory stimuli produced painful sensations. That a lesion of the posterior columns might produce "central pain" is a remote but unlikely possibility.

The thalamus, lesions of which give the classic picture of "central pain" and other forms of subjective sensory disturbances, was implicated in four cases. Superficial sensation (pain, touch and temperature) was impaired in most of these cases. This, best demonstrated in the first case, is of significance, as in most of the cases recorded in the literature there was more impairment of the deeper than of the superficial forms of sensibility. In our first case a small vascular lesion was confined to the posterior part of the external nucleus of the thalamus along its inferolateral surface. In the other three cases the thalamic involvement was due to compression by neoplasm (cases 2 and 3) and an aneurysm (case 4). In case 3 the left side of the pulvinar was invaded by the neoplasm. The involvement of the parietal portion of the cortex in the last three cases leaves open the question whether the subjective sensory disturbances may not have been

of cortical origin. The simultaneous implication of the thalamus, however, induced us to consider that structure to be responsible for the "spontaneous pain" and hyperaffectivity in this group.

Of greatest interest are our last two cases in which subjective sensory disturbances, consisting of "spontaneous pains" and "feelings like electricity" associated with impairment of the superficial and deep modalities of sensation, were of cortical origin. In both of these cases there was destruction of the postcentral and superior parietal convolutions and the thalamic nuclei were completely spared. From these two cases and the few previously recorded by Mills and others it can be concluded that the cerebral cortex is concerned not only with sensory discrimination but also with appreciation of the more primitive types of sensations, disturbances of which are associated with some of the phenomena previously mentioned.

We have submitted data which tend to indicate that "spontaneous pain" and hyperpathia are associated in most cases with incomplete lesions of the spinothalamic tract or its components. Irritation or incomplete destruction of the spinothalamic sensory system may give any one or a group of the phenomena discussed in this presentation.

EFFECTS OF TOTAL REMOVAL OF THE CEREBRAL CORTEX

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We previously reported (Culler and Mettler [1]) success in the attempt to establish a motor conditioned reflex to sound and light in an animal from which the cerebral cortex had been removed. The present report is designed to extend these findings and also to point out that animals from which the cortex has been removed exhibit physiologic changes which cannot be explained simply in terms of impaired somatic motor and sensory function.

The evidence presented here was obtained from a study of an animal operated on in four stages during a period of six months. The observations were made from two to four months after the last operation and about nine months after most of the cortex had been removed. At the end of this time the animal was in excellent condition and was killed for morphologic study. At indicated points we have taken the liberty to draw on unpublished laboratory records for amplifying remarks concerning the early behavior of animals of this type.

OBSERVATIONS

Autopsy.—The entire cerebral cortex was either ablated or disconnected from the underlying structures (fig. 1). The caudate nuclei on both sides were injured, and the thalamic nucleus on the left side was injured. The lateral geniculate bodies had been invaded by fibrous connective tissue.

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1. Culler, E. A., and Mettler, Fred A.: Observations upon the Conduct of a Thalamic Animal, Proc. Soc. Exper. Biol. & Med. **31**:607, 1934; Conditioned Behavior in a Decorticate Dog, J. Comp. Psychol. **18**:291, 1934.

Sensory System.—Directly after operation for removal of the cortex animals of this type evince no appreciation of sound or light. Sensitivity to tactile and painful stimuli is depressed. Gradually the tactile sense becomes more acute, especially sensitivity in the muzzle. Responses to auditory stimuli return suddenly (on the ninth or tenth day, as H. Rothmann [2] and M. Rothmann [3] observed). The olfactory and gustatory sensations may be present. Some of our animals apparently sniffed about; however, we agree with H. Rothmann that this was a utilization of sensibility in the muzzle rather than olfaction, since no correlation between such movements of the head and respiratory excursions occurred. After its initial sudden appearance auditory perception became gradually more acute. In this experimental animal not only were we able to demonstrate a reaction to gross sounds but we were able to establish a conditioned retraction of the hindlegs (the pelvis being fixed) to sounds having a certain degree of attenuation. Our normal dogs could hear the test sound when it was attenuated to about 130 decibels. The decorticate animal could hear the sound provided it was not attenuated beyond 60 decibels. It is doubtful if the animal could hear sounds much weaker than this. We were never able to show that the dog could localize the source of the

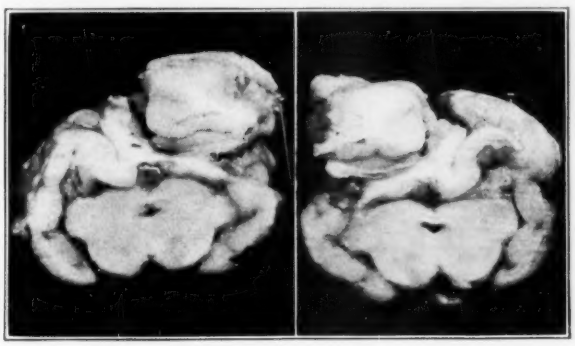

Fig. 1.—The brain of the animal studied. The cortex was removed or was so undercut as to eliminate its functional value. Microscopic study revealed all cortical connections except those from the rhinencephalon to have been severed.

sound, but we found it possible to show that the dog could distinguish between two types of sound. A conditioned reflex to a 1,000 cycle tone was established, the animal not reacting to a bell of weaker, equal or louder intensity than the tone. The tonal conditioned reflex was then extinguished, and it was possible to establish a conditioned response to the bell, the animal not reacting to the 1,000 cycle tone when this was of weaker, equal or stronger intensity.

Proprioception remained dulled, as evinced by the assumption of bizarre postures while standing and by occasional walking on the dorsum of the forepaw.

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2. Rothmann, H.: Zusammenfassender Bericht über den Rothmannschen grosshirnlosen Hund nach klinischer und anatomischer Untersuchung, Ztschr. f. d. ges Neurol. u. Psychiat. **87**:247, 1923.

3. Rothmann, M.: Erkrankungen des Grosshirns, Kleinhirns, der Brücke und der Hirnhäute, in Mohr, L., and Staehelin, R.: Handbuch der inneren Medizin, Berlin, Julius Springer, 1912, vol. 5, p. 294; Demonstration des Sektionsbefundes des grosshirnlosen Hundes, Neurol. Centralbl. **31**:867, 1912.

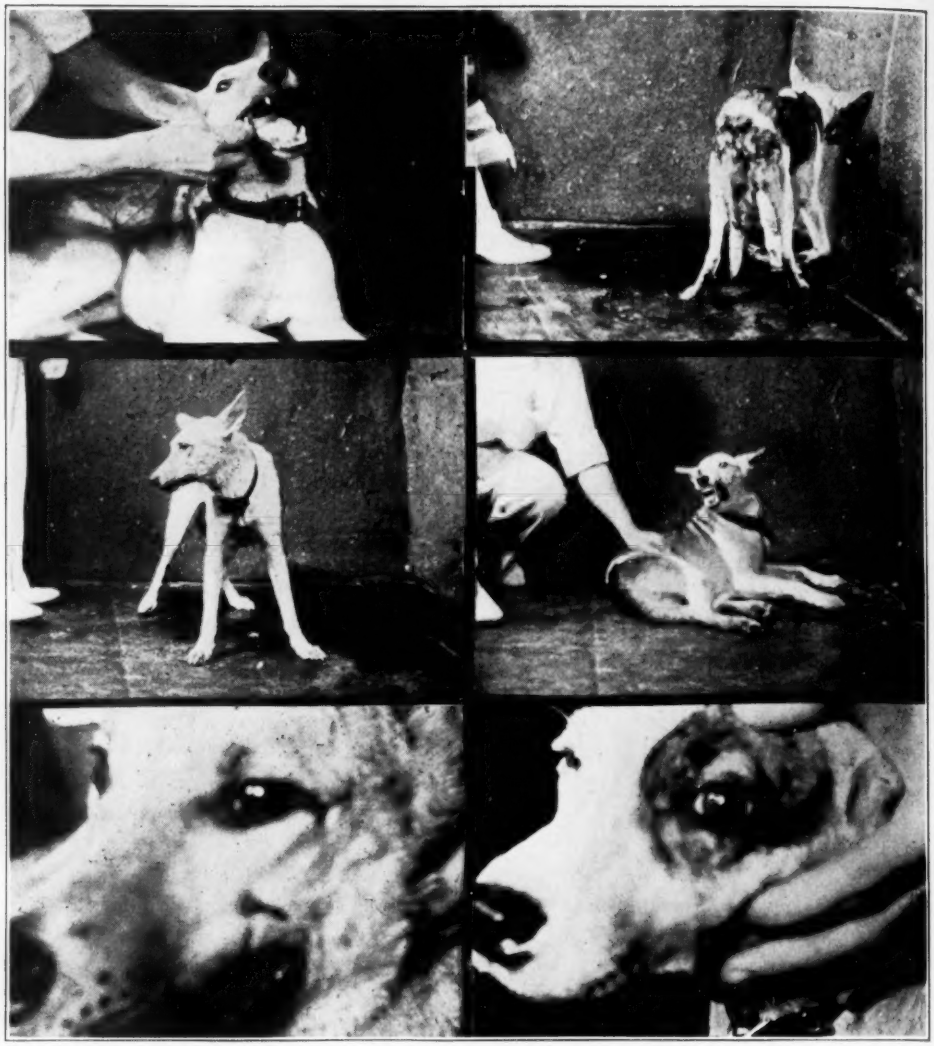

Fig. 2.—Enlargements of motion picture film (16 mm.) taken of the decorticate animal. In the upper left-hand photograph the animal is shown in the process of chewing, which was regularly initiated by pressing a piece of meat between the premolars. In the upper right-hand photograph the animal is shown after it had walked against a wall. This is not an artificially posed picture but represents an actual incident of locomotion. After reaching the wall the animal stood barely touching it for a few moments; as it attempted to move away the right forepaw turned over, and the animal remained in this position for some time. It shows one of the many bizarre positions assumed by the animal and the disregard shown toward proprioceptive stimuli. Observe the position of the tail and the abduction of the left hind extremity at the metatarsal articulation. In the middle photograph on the left the dog is shown in the standing position from the front. Note the abduction of the extremities and the wide base. In the middle photograph on the right the dog is shown reacting to a contact on the flank. The reaction began with a snarl and ended with the dog's biting viciously at the place stimulated. The movements were very rapid. This is an exhibition of the animal's irritability. In the lower left-hand photograph the pupils of the decorticate animal are compared with those of a normal dog, shown in the lower right-hand photograph. The illumination used was identical and of the usual flood-light type employed for motion-pictures. The heads were not quite the same distance from the camera, so that the picture of the decorticate dog is somewhat relatively larger than that of the normal animal. Observe the dilatation of the pupil of the decorticate dog.

Tactile sensibility returned gradually, until in one animal it was probably the most acute sense. Conditioned reflexes were also established to thermal stimuli, as well as to tactile stimuli. Attempts to establish a conditioned reflex to visual stimuli were unsuccessful in this animal. The changes observed at autopsy (invasion of the lateral geniculate bodies by fibrous tissue), however, were doubtless responsible for this failure, since in animals in which no injury to the geniculate bodies is present it is possible to establish conditioned reflexes to visual stimulation.[1]

Motor System.—Immediately after operation a decorticated animal lies prostrated and quiet but it may, as soon as the hypnotic wears off, show incessant motion of the extremities, as when running. The animal cannot support its weight, but there may be pronounced extensor rigidity. Breathing is depressed and stertorous. The animal will not eat or swallow, and there appears to be some pharyngeal collapse. On the second day it may be able to stand, but usually it sinks gradually under its own weight to the floor. Incessant activity rarely may persist and must be controlled by hypnotics. We found that our animals were able to walk slowly in from three (Goltz [4]) to five (Zeliony [5]) days. Ability to swallow (if fluids are introduced in the region of the fauces and the head is elevated) returns in about five days.

Respiration remains depressed, and activity only slowly begins to increase. It is important to note the absence of anything which might be described as incessant activity once the postoperative excitation wears off. Extreme lethargy is the characteristic picture, and when the animal is standing a peculiar propped-up appearance is observed. This includes an increased floor base between the legs. The tail is held between the legs, and the head is held low, with the snout touching the floor. Examination of the extremities reveals the lengthening reaction or clasp-knife reflexes (Walshe [6]).

All motion is progressive, and if the dog gets into a corner, only by the accident of falling to one side will it get out. When confronted with an impasse, such as an obstruction, slow progressive movements yield to a distressed pushing. This excitation, beginning with random movements of the head, gradually spreads down the cervical region of the spine (arguing for the existence of a diffuse path in the absence of the pyramidal tract) until the forelegs and the hindlegs are successively involved. This may become pronounced enough to cause violent thrashing about, by which the animal generally gets out of the immediate difficulty. After the eleventh day the animal shows a tendency to stop when its muzzle comes in contact with an object and not to push forward. Any attempt to impress a movement on the dog is met by resistance. If the animal is pushed backward it tries to go ahead, and if pulled forward it pulls back violently (the only condition in which animals in a semiacute condition back up). There is never any tendency on the part of the animal to initiate a movement suddenly (except in the case of reflexes, such as the righting reflex), but activity always

4. Goltz, F.: Ueber die Verrichtungen des Grosshirns, Arch. f. d. ges. Physiol. **13**:1, 1876; **14**:412, 1877; **20**:1, 1879; **26**:1, 1881; **34**:451, 1884; **42**:419, 1888; Hund ohne Grosshirn, ibid. **51**:570, 1892.

5. Zeliony, G. P.: The Dog Without a Forebrain, Tr. Soc. Russ. Physicians, St. Petersburg, 1911, pp. 3 and 13.

6. Walshe, F. M. R., and Robertson, E. G.: Observations upon Form and Nature of "Grasping" Movements and the "Tonic Innervation" Seen in Certain Cases of Lesion of the Frontal Lobe, Brain **56**:40, 1933.

begins slowly and gradually gains momentum. When activity is in progress there is likewise never a sudden stopping of the motion, but this dies down gradually. Thus there is a specific difficulty in activating or inhibiting movement suddenly. When the animal attempts to lie down, this cannot be accomplished without difficulty. As the limbs are partially relaxed and the body sinks slightly, the passive extension of the extensor muscles produces a reflex activation which causes the dog to stand upright again, reminding one of an elastic decrement curve. This process may go on for hours. If the animal is taken up at such a time and laid on its side, it rapidly scrambles back to its feet (Zeliony also made this observation).

Movements of the head and body could be evoked in the decorticate animal by shining a flood-lamp suddenly in the eyes. Conjugate deviation of the eyes in all directions was observed, usually in relation to turning of the head and neck, but it also occurred when the head was fixed.

Convulsions occur in certain animals. These appear usually after the fourteenth day and present rapid tumblings about the transverse axis of the body. Epileptiform seizures of the muscles of the head and neck, with twitching of the muzzle and rapid snapping of the head to one side, were occasionally observed.

Autonomic System.—Pupillary Diameter: Directly after operation pupillary reflexes are abolished, but they soon return and on the ninth day are definitely observable, as is the crossed reflex.

Under identical light conditions and in animals of the same size the pupillary diameter was: in the decorticate animal, 10 mm., equal in the two eyes; in an animal from which both occipital lobes only had been removed, 3 mm., and equal; in an animal in which one hemisphere only had been removed, 4 mm., and equal (very strong light brought out inequalities), and in a normal animal, 2 mm. and equal. When the illumination was reduced so that the normal dog's pupils dilated to 4 mm., the pupils of the decorticate animal did not dilate further. When, however, the illumination was increased the pupils of the decorticate dog constricted before those of the normal animal, giving a measure of 4 mm. for the former and 2 mm. for the latter. Under the influence of a miotic (physostigmine or pilocarpine) injected into the animal, pupillary fluctuation without constriction of a sustained type was noted. When the drug was instilled into the conjunctival sac a typical result was produced. If the animal relaxed while under the influence of a miotic systemically administered, the pupils constricted excessively. When the animal was touched or aroused in any way the constriction disappeared and was replaced by dilatation. It was impossible to measure these changes, since measurement necessitated rousing the animal.

Temperature of the Body: No marked difference from the temperature of a normal dog was observed in that of the decorticate animal, which ranged around 101 F. After active exercise for about an hour the temperature occasionally rose as high as 105 F. During rest it was once found to be as low as 99.6 F. When the animal was placed in a moderately cool environment (about 50 F.) the temperature of the body was maintained at 101 F., and the animal shivered mildly under such circumstances. When the dog was placed in a hot environment the temperature of the body did not stay at 101 F. but rose moderately (102 F.), although it apparently could not be forced very high. When the temperature was raised to 105 F. by exercise and the animal was then plunged in cold water, shivering commenced when the temperature had fallen to 103 F. It is possible

that this may be interpreted according to Nafe's[7] theory of appreciation of temperature. In general, the impression was that the animal was able to maintain its temperature and eliminate heat, although its reactions in these respects, especially in the elimination of heat, were not as prompt as those of a normal animal. Unfortunately, no facilities for obtaining low environmental temperatures were available.

Digestive Tract: The feces of the animal were not uniform and were made up of a loose watery discharge in which well formed elements occurred. If large quantities of food (ground beef) were given, the animal continued to swallow the food presented until regurgitation occurred. Under such conditions a residuum amounting to from 0.5 to 1 Kg. remained unregurgitated. With fluids the animal exhibited a tendency to stop drinking after a time. When food was withheld for several feeding periods there was greater avidity when the food was presented. The characteristic postures assumed during defecation were interfered with by the inability of the animal to keep its balance, and the position assumed during urination (the animal was a mature male) was crouching, with flexion of all four extremities.

At autopsy the enteral passages were found to be strongly contracted. No gastroduodenal ulcers were observable in this animal, and few parasites were present.

Nutrition and Growth: Before operation the animal weighed 10.4 Kg. In the course of the operative procedures the weight increased by apparently normal growth processes to 14.5 Kg. after the second operation and stayed at this level for more than six months, at which time the dog was killed. The animal appeared much stronger and hardier than other animals of its size, weight and breed. Wounds of the skin healed quickly and resisted suppuration.

Heart Rate: Over a large series of measurements under various conditions this animal's heart rate was faster than that of a normal animal more than 93 per cent of the time. (The normal animal was kept under identical conditions of living and feeding and was chosen with care to approximate the decorticate animal in size.) The heart rate was usually between 90 and 100 beats per minute, but it rose occasionally during excitement to over 160 and fell sometimes during sleep to 40. The animal presented a marked sinus arrhythmia, which became especially pronounced on the injection of ephedrine.

Blood: A blood count revealed an abnormal picture. There was no evidence of a pathologic process to which it might be related. The following observations are presented in comparison with the averages of eighteen readings obtained on four dogs without cortical ablation (three of which had been subjected to large doses of roentgen rays):

Animals	White Blood Cells	Red Blood Cells	Hemoglobin, Percentage
Normal dogs.....	11,242	5,585,000	92 (Dare
Decorticate dog.....	19,350	3,670,000	70.6 (Newcomer)

The highest white count in our records for undiseased animals is 13,950; the lowest red blood cell count is 4,480,000, and the lowest percentage of hemoglobin is 84 (Dare). The differential white cell count for the decorticate dog was: lymphocytes, 19 per cent; monocytes, 0.5 per cent; polymorphonuclears, 77.5 per cent, and eosinophils, 3 per cent.

7. Nafe, J. P.: Handbook of General Experimental Psychology, edited by C. Murchison, Worcester, Mass., Clark University Press, 1934, p. 1037.

At autopsy the spleen was found to be enormously distended with blood and displaced. Few parasites were found at autopsy. Microscopic study of the spleen and lymph nodes in this animal revealed that with regard to both mononuclears and polymorphonuclears there was a shift to the left. The spleen showed considerable stasis but no evidence of an abnormal destruction of erythrocytes. There was an increase in the number of polymorphonuclears in the spleen.

Sugar Content of the Blood: On June 7, 8, 9 and 10 the animal was fed water, milk, raw meat and suet, and on June 11 a test for tolerance for dextrose was carried out following a fast of eighteen hours. The determinations were made by the method of Folin and Wu, following precipitation by the Haden (1923) modification. For the test meal 2 Gm. of dextrose per kilogram of body weight was administered orally. An initially low level of blood sugar was noted (66 mg. per hundred cubic centimeters), but the feeding of dextrose caused a definite increase in the sugar content (in thirty-six minutes, 122 mg. per hundred cubic centimeters; in seventy-five minutes, 145 mg.; in ninety-nine minutes, 142 mg.;

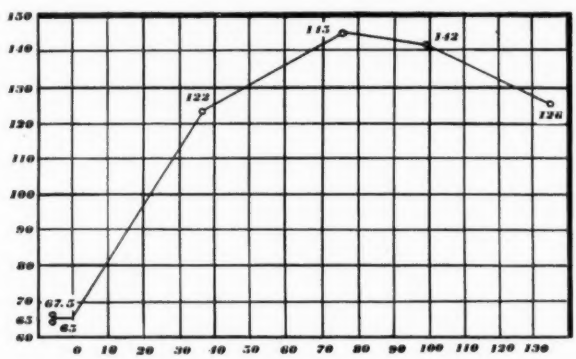

Fig. 3.—A diagram showing reducing substances present in blood after the oral administration of dextrose (2 Gm. per kilogram of body weight). Determinations were made by the method of Folin and Wu. Notice the initial low level for sugar, based on two tests on the same sample of blood. At zero the dextrose was administered. The curve, it should be noted, remains elevated for a longer time than would be expected for an animal with an initially low sugar content. The time in minutes is shown on the abscissas, and the concentration of the reducing substances in milligrams per hundred cubic centimeters of blood is shown on the ordinates.

in one hundred and thirty-five minutes, 126 mg.), which remained elevated longer than usual, indicating a latent disturbance in the sugar metabolism (fig. 3).

When it was observed that the blood sugar content after fasting was low, it was decided to test the approximate level of the renal threshold for dextrose. After heavy feeding on the night of June 11, 30 Gm. of dextrose was administered the following day at 4:30 p. m. At 7:30 the urine was normal according to the Benedict method, and at 8:15, 100 Gm. more of dextrose was given. At 10 p. m. the animal was catheterized, after considerable struggling, and the urine was found to contain about 1 per cent of reducing substance. At noon on June 13, the animal not having voided meanwhile, the bladder was voluntarily emptied, and the urine was found to contain somewhat less than 1 per cent of reducing

substances. At 12:15, 60 Gm. of dextrose was given by mouth, and at 6 the urine gave a negative reaction to Benedict's solution. On June 14 the animal was put into a stock, and after being allowed to struggle for fifteen minutes the urine was again tested and was found not to contain sugar. Following several days of adequate feeding, blood was drawn on June 18 after a twenty-one hour fast. In this instance it was impossible to draw blood without strapping the animal in the stocks, so violent was the behavior. The blood when tested according to the Folin-Wu method on a Haden filtrate gave a value for sugar of 72.5 mg. per hundred cubic centimeters, and a filtrate prepared according to Somogyi's method, run at the same time, a value of 65 mg. Simultaneously a test for nonprotein nitrogen showed a value of 25 mg. of nitrogen per hundred cubic centimeters. On another occasion it was possible to raise the sugar content after fasting to 94 mg. by thirty minutes of exercise under excitation. If ephedrine (5 mg. per kilogram) was then injected, the sugar content rose in another thirty minutes to 125 mg. The administration of 18 units of insulin (1.24 units per kilogram) gave rise to hypoglycemic symptoms, though in a control animal no symptoms were produced. If the insulin was given over a period of time instead of as a single dose, no hypoglycemic symptoms occurred.

The serum calcium in the decorticate animal was 12.2 mg. according to the Clark-Collip modification of the Kramer-Tisdall test, which was an increase over the normal values for dogs.

Action of Drugs: The animal showed a marked susceptibility to the action of drugs. This action was prominent in the case of sympathomimetic and parasympathomimetic drugs (Mettler and Culler [8]).

Capacity for Muscular Exertion: It might be contended that many of the characteristics of this animal were the necessary concomitants of general cachexia. While it cannot be denied that the anemia and the low sugar content of the blood must have played a part in the general reactions of the animal, nothing could be farther from the facts than to suppose that the animal was feeble and weak. On the contrary, its strength and endurance were remarkable, as became apparent to those who had occasion to handle the dog.

In order to obtain some objective measure of this capacity for sheer exertion, the animal was caused to lift a lever against a stiff steel spring. The lever was strapped to the right forepaw, and flexion of the extremity was insured by shocks delivered to the paw at fifteen second intervals. The excursions of the lever were measured by a work adder, which gave in a rough way the amount of work done by the right anterior extremity in flexion against the pull of the spring. A larger and very active animal chosen for its known vitality was then subjected to the same test. The results were as follows: in the decorticate dog, weight 14.5 Kg. and crown-rump length, 70 cm., and in the control dog, weight 20 Kg. and crown-rump length, 75 cm. During a fourteen minute period the control did only 75.5 per cent as much work as the decorticate animal, despite the larger size of the former. The control animal was exhausted, but the decorticate dog was not. The aforementioned figures, it should be pointed out, are necessarily crude and are offered not in an attempt to make an absolute statement of work in terms of gram centimeters but to dispel the idea that the animal's general physiologic reactions can be explained in terms of poor condition in the sense of physical weakness.

Blood Pressure: A determination of the blood pressure was made by the direct method, with the dogs under pentobarbital sodium anesthesia. A value of 80 mm.

8. Mettler, Fred A., and Culler, Elmer: Action of Drugs on the Chronic Decorticated Preparation, J. Pharmacol. & Exper. Therap. **52**:366, 1934.

of mercury systolic and 75 mm. diastolic was obtained. For the decorticate animal approximately 1 cc. of pentobarbital sodium (for veterinary use) per 5 pounds (2.3 Kg.) of body weight was used. This gave a light narcosis which was equivalent to that of the control animal, to which 1 cc. of the anesthetic per 4 pounds (1.8 Kg.) of body weight was given. The control animal showed a systolic value of 90 mm. and a diastolic value of 80 mm. (The control animal used in this test had not been subjected to the administration of any drugs other than pentobarbital sodium and weighed 24.9 Kg.)

The administration of ephedrine sulphate (5 mg. per kilogram of body weight injected intramuscularly) produced in the control animal a rise in systolic pressure to 140 mm. and in diastolic pressure to 120 mm.; these measurements were taken ten minutes after the injection of the ephedrine. In the decorticate animal the same dosage of ephedrine sulphate produced a rise in systolic pressure to 132 mm. and in diastolic pressure to 126 mm. within ten minutes after the injection, the pressure falling away from the peak somewhat thereafter.

The pulse pressure of the decorticate dog was therefore 5, and that of the control animal, 10. After the injection of ephedrine the decorticate dog's pulse pressure was 6, and that of the normal animal, 20.

COMMENT

Although the literature contains evidence to the contrary (Dresel,[9] H. Rothmann,[2] M. Rothmann,[3] Zeliony [10]), it is still common to encounter the impression that decortication produces blindness and deafness identical with those produced by destruction of the peripheral apparatus. It is true that what appears to be complete abolition of the senses exists during the first week after decortication, but this condition suddenly disappears in about ten days and yields to a high threshold of sensation (Culler and Mettler;[1] Mettler, Finch, Girden and Culler [11]). We therefore conclude that subcortical centers are capable of sensory appreciation.

The inability to activate and inhibit movements suddenly seems to show that this is one of the functions of the cortex as mediated through the cerebrospinal tracts. The fact that shortly after decortication the origination of somatic movements occurs in a diffuse way and spreads relatively slowly down the spinal cord seems to point to the existence of an intrinsic spinal mechanism, such as was postulated by Creed, Denny-Brown, Eccles, Liddell and Sherrington,[12] which is available to thalamic excitation.

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9. Dresel, K.: Die Funktionen eines grosshirn-und striatumlosen Hundes, Klin. Wchnschr. **49**:2231, 1924.

10. Zeliony, G.: Observations sur des chiens auxquels on a enlevé les hémisphères cérébraux, Compt. rend. Soc. de biol. **65**:707, 1913. Footnote.[4]

11. Mettler, Fred A.; Finch, Glen; Girden, Edward, and Culler, Elmer: Acoustic Value of the Several Components of the Auditory Pathway, Brain **57**:475, 1934.

12. Creed, R. S.; Denny-Brown, D.; Eccles, J. C.; Liddell, E. G. T., and Sherrington, C.: Reflex Activity of the Spinal Cord, New York, Oxford University Press 1932.

The hypertonia of decorticated dogs (especially those observed in a semi-acute or acute experiment) has much in common with that usually described as "decerebrate" (Davis,[13] Davis and Pollock[14]). Dandy[15] stated that there is no evidence of spasticity in dogs after the removal of one hemisphere, but we have often observed it in animals used in semi-acute experiments. The hypertonia in such animals is chiefly in the extensor muscles, although the tonus of the flexor muscles is also somewhat increased.

It is difficult to understand how the idea that incessant activity is characteristic of the decorticate animal came to be prevalent. There were intimations in Goltz'[4] work that such a condition occurred in his animals, but M. Rothmann's animal exhibited long periods of quietude, and Zeliony found the characteristic picture to be sleep or simple standing and remarked that he never saw his animal run. Dresel made no mention of incessant activity, and we have been at some pains to show that excitation occurs only under well defined circumstances. The level of excitability fluctuates considerably, often being depressed for many days. We noticed this to occur when conditions were kept as constant as possible over periods of weeks. It may be related to variations in temperature, especially warmth.

That the autonomic nervous system is influenced by the cortex is indicated by a large body of evidence (Kohnstamm,[16] Pavlov,[17] Kuntz[18]), but the nature of this influence is far from clear. It has been shown that the hypothalamus is concerned with sympathetic (Bard;[19] Beattie, Brow and Long;[20] Brown,[21] Fulton;[22] Fulton and

13. Davis, L. E.: Decerebrate Rigidity in Man, Arch. Neurol. & Psychiat. **13**: 569 (May) 1925.

14. Davis, L. E., and Pollock, L. J.: Studies in Decerebration: III. The Labyrinth, Arch. Neurol. & Psychiat. **16**:555 (Nov.) 1926. Pollock, L. J., and Davis, L. E.: Studies in Decerebration: An Acute Decerebrate Preparation, Arch. Neurol. & Psychiat. **12**:288 (Sept.) 1924.

15. Dandy, W. E.: Physiological Studies Following Extirpation of Right Cerebral Hemisphere in Man, Bull. Johns Hopkins Hosp. **53**:31, 1933.

16. Kohnstamm, O.: Physiologie und Pathologie des viszeralen Nervensystems, in Mohr, L., and Staehelin, R.: Handbuch der inneren Medizin, Berlin, Julius Springer, 1912, vol. 5, p. 1016.

17. Pavlov, I.: Conditioned Reflexes, New York, Oxford University Press, 1927; Lectures on Conditioned Reflexes, New York, International Publishers Co., Inc., 1928.

18. Kuntz, A.: Autonomic Nervous System, ed. 2, Philadelphia, Lea & Febiger, 1934.

19. Bard, P.: Diencephalic Mechanism for Expression of Rage with Special Reference to the Sympathetic Nervous System, Am. J. Physiol. **28**:490, 1928; Central Representation of the Sympathetic Nervous System as Indicated by Certain Physiological Findings, in Vegetative Nervous System, Association for Research in Nervous and Mental Diseases, Baltimore, Williams & Wilkins Company, 1930.

(Footnotes continued on next page)

Ingraham [23]) and parasympathetic (Kabat, Magoun and Ranson [24]) activity. It has also been shown that the cortex projects fibers on these critical lower areas (Mettler,[25] Kuntz [18]), but it is not known whether the cortex inhibits or activates both divisions of the autonomic system or exerts its influence primarily on one division. It would be expected that the decorticated animal would contribute evidence useful in the solution of this question. That disturbances of the autonomic nervous system are present in these animals is apparent not only in the sense of those disturbances which follow any operation but also in obviously different disturbances, such as digestive difficulties. Zeliony [5] also observed a suppression of psychic secretion in his animal during the first month following decortication but apparently attached no importance to it.

The level of blood sugar in this animal is of especial interest. Dresel [9] showed that immediately following decortication the sugar content rose but that within ten days it returned to the normal level. He attributed the disturbance of the carbohydrate metabolism to removal of the corpus striatum. Evans [26] assumed on the basis of work by Bulatao and Cannon [27] that removal of the cortex causes prolonged hyperglycemia and glycosuria and "a sustained condition of excitation of the whole sympathetic nervous system, one of the consequences of which is a maintained outpouring of adrenalin into the blood." Bulatao and Cannon, however, concluded from the results of their work that extensive cerebral destruction (not pure decortication) causes an affective state which influences the sugar content over a period of several hours. We are unable to support Evans' view of pure and sustained sympathetic overactivity but believe that a definite disturbance caused by release of both the sympathetic and parasympathetic system exists after total ablation of the cortex.

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20. Beattie, J.; Brow, G. R., and Long, C. N. H.: Physiological and Anatomical Evidence for Existence of Nerve Tracts Connecting Hypothalamus with Spinal Sympathetic Centres, Proc. Roy. Soc., London, s. B. **106**:253 (May 3) 1930.

21. Brown, C. W.: Central Nervous Mechanism for Emotional Responses: I. Some Limitations of Previous Investigations with Suggestions for Further Experimental Work, J. Comp. Psychol. **14**:365 (Dec.) 1932.

22. Fulton, J. F.: New Horizons in Physiology and Medicine: Hypothalamus and Visceral Mechanism, New England J. Med. **207**:60, 1932.

23. Fulton, J. F., and Ingraham, F. D.: Emotional Disturbances Following Experimental Lesions of Base of Brain, J. Physiol. **67**:XXVII, 1929.

24. Kabat, H.; Magoun, H., and Ranson, S. W.: Electrical Stimulation of Hypothalamus, Proc. Soc. Exper. Biol. & Med. **31**:541, 1934.

25. Mettler, Fred A.: Main Association and Efferent Fiber Systems of the Cerebral Cortex in Primates, Thesis, Cornell University, 1933.

26. Evans, C. L., in Starling, E. H.: Principles of Human Physiology, ed. 6, Philadelphia, Lea & Febiger, 1933.

27. Bulatao, E., and Cannon, W.: The Rôle of the Adrenal Medulla in Pseudoaffective Hyperglycemia, Am. J. Physiol. **72**:295, 1925.

Observations at autopsy on our decorticate animal revealed a notable increase in the size of the pancreas. Detailed and laborious counts made on this tissue in conjunction with that on the pancreas of normal animals showed a decrease in the unit size of the individual islands of Langerhans in the decorticate animal far beyond any normal variation.

In earlier studies we were much puzzled and disturbed by the anorexia, dysphagia and eventual cachexia displayed by animals following various operations on the cortex. We now know that removal of the cortex of the frontal lobe alone is sufficient to produce a disturbance in gastro-intestinal function and have been able to produce erosion of the gastric mucosa by this means (Combs, Mettler, Spindler and Mettler [28]).

CONCLUSIONS

1. The "chronic" decorticated animal is able to distinguish light from darkness, to appreciate warmth and tactile sensation and to hear. The ability to hear extends to distinction between sounds which are qualitatively different and extends over a fairly large range of intensity, although the threshold is high.

2. The decorticated animal exhibits physiologic changes referable to vegetative function and not explainable in alteration of the somatic motor and sensory functions.

3. The decorticated animal does not exhibit incessant activity but shows an inability to initiate or inhibit movement suddenly. The distribution of tonus is abnormal, and posture is disturbed.

4. The decorticated animal exhibits a low sugar content of the blood, with an altered tolerance for dextrose, a high calcium content, increased sensitivity to the action of drugs and disturbed gastro-intestinal function. There is an abnormal blood picture with decrease in the erthrocyte count. The pulse pressure is small.

5. Evidence is presented which leads us to the conclusion that both the sympathetic and the parasympathetic system are normally inhibited by the cortex and that removal of the cortex releases both of these systems.

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28. Combs, J. D.; Mettler, F. A.; Spindler, James, and Mettler, Cecilia C.: Disturbances in Autonomic Function Following Localized Cortical Ablations, Anat. Rec. (supp.) **61**:11, 1935.

MESENCEPHALIC GLIOMA

A CLINICAL AND PATHOLOGIC ANALYSIS OF TEN CASES

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An infiltrating tumor at the base of the brain offers serious difficulties in diagnosis. This is particularly true in cases of tumor involving the mesencephalon, in which the few signs of an indeterminate nature make the establishment of a diagnosis practically impossible. Even with the aid of injections of air one often fails to differentiate a tumor of the mesencephalon from one of the cerebellum. For this reason it may be valuable to review the various syndromes associated with tumors of the mesencephalon in order, if possible, to establish some diagnostic criteria of value.

REPORT OF CASES

The first feature which strikes one on reviewing the syndromes associated with tumors of the mesencephalon is the fact that there is no constellation of signs and symptoms which can be said to be present in all cases of tumor in this region. This is not surprising in view of the many structures in this portion of the brain, the clinical features of the case depending, of course, on the number of structures invaded and the degree of their involvement. Generally speaking, there are two groups of cases; one with few signs, in which the tumor is confined largely to the tectum of the mesencephalon and one with more numerous signs, in which the glioma occupies the tegmentum and basis mesencephali. Depending on whether one portion of the mesencephalon or the other is involved by the tumor, the clinical picture varies perceptibly.

Group 1: Cases of Glioma Involving the Tectum Mesencephali.—Our study included three cases belonging in this group.

CASE 1.—*Headaches and failing vision for five years. Spasms of the right side of the face. Sluggishness of the pupils; choking of 3 diopters in each eye; constriction of fields with beginning left homonymous hemianopia. Enlargement of the sella turcica. Glioma involving the colliculi and obstructing the aqueduct of Sylvius.*

History.—L. D., a girl aged 19, entered the University Hospital on Feb. 8, 1929, with a complaint of failing vision. She had suffered from frontal headaches

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for over five years and during the same period had found that vision was failing. In the past two and one-half years she had had seizures in which the right side of the face drew up and the right eye closed; these attacks lasted from three to four minutes. She had noticed occasional ringing in the right ear. There was no history of diplopia, loss of hearing or unsteadiness of gait.

Examination.—The patient was obese, weighed 180 pounds (81.7 Kg.) and was rather retarded mentally. Neurologic examination revealed few signs. The patient was unable to identify odors on either side and, in addition, claimed that she smelled foul odors. The pupils were of medium size and reacted sluggishly to light and in accommodation. The visual acuity was 6/30 in the left eye, but the patient counted fingers at a distance of only 4 feet (120 cm.) with the right eye. The visual fields showed a left homonymous defect. There was no internal rotation of the right eye in tests for convergence, but when the opposite eye was closed the right internal rectus muscle functioned normally. There was 3 diopters of choking in each eye. Otherwise neurologic examination gave negative results.

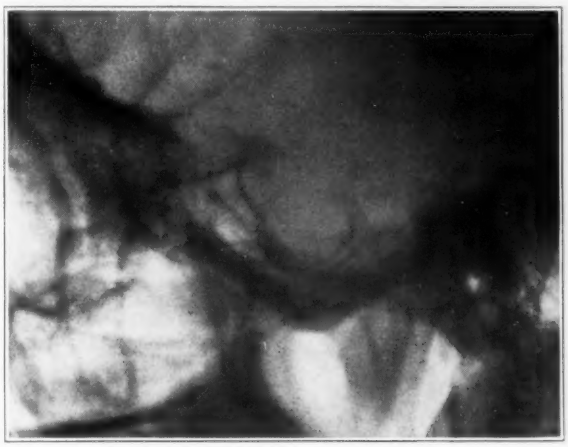

Fig. 1. (case 1).—Roentgenogram showing a greatly enlarged sella turcica, measuring 10 mm. in anteroposterior direction and 16 mm. in depth.

A watch was heard at a distance of 20 inches (50 cm.) in each ear. There were no reflex or sensory disturbances, and there was no disturbance of associated movements of the eyes. Fine unsustained nystagmus was elicited by having the patient look to the left or upward. Serologic tests of the blood and spinal fluid gave negative results.

Roentgenograms: There were increased convolutional markings of the skull with considerable separation of the sutures. The posterior clinoid processes were eroded, and the sella turcica was enlarged, the measurements being 16 by 10 mm. (fig. 1).

Operation.—On March 1, 1929, a transfrontal craniotomy on the right side was performed but failed to expose the tumor. The patient reacted poorly and died on the day after operation.

Necropsy.—A small glioma was invading the collicular region, the floor of the third ventricle and the posterior commissure and blocking the iter (fig. 2). It invaded also the pulvinar thalami. Both of the posterior colliculi were affected.

but only the right superior colliculus was involved. The posterior commissure was many times the normal size, and the nucleus of the third nerve in the floor of the aqueduct was invaded. The following structures were not penetrated by the glioma: the lateral geniculate body, temporal lobe, occipital lobe, lateral lemniscus, medial geniculate body, nucleus of the eighth nerve, red nucleus and superior cerebellar peduncle.

CASE 2.—*Severe frontal headaches for five months before entrance. Four generalized convulsions. Choked disk of 2 diopters in each eye, and enlargement of the head. Slight right side exophthalmos with enlargement of the palpebral fissure, right homonymous hemianopia; signs of cerebellar involvement, endocrine disturbances and mental retardation. Roentgen signs of increased pressure with enlargement of the sella turcica. Obstruction in the aqueduct revealed by ventriculogram. Operation without exposure of the tumor. Glioma invading the right inferior colliculus and involving also the left colliculus.*

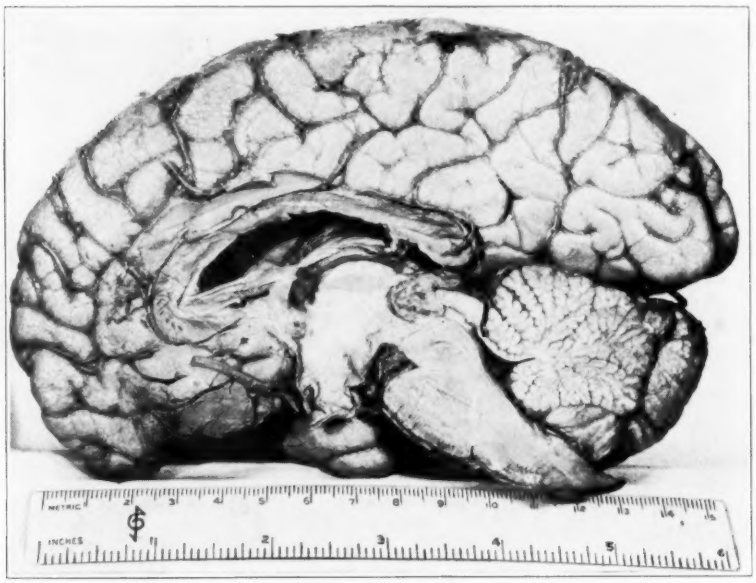

Fig. 2 (case 1).—Section of the brain showing a small tumor in the tectal portion of the mesencephalon, arising from the posterior commissure

History.—M. R., a girl, aged 12, entered the University Hospital on March 15, 1930, with a complaint of headache and generalized convulsions, both of which had been present for five months before entrance. There were no other significant symptoms. She had had four convulsions in all. There was no history of diplopia, hemianopia, tinnitus, loss of hearing or unsteadiness of gait.

Examination.—There was slight exophthalmos on the right side with some widening of the right palpebral fissure. There was subsiding choked disk of 2 diopters in each eye. The visual acuity was 6/24 in each eye, and the visual fields showed right homonymous hemianopia. Extra-ocular movements and all types of pupillary reactions were normal. No test of hearing was recorded. In

addition there were signs of cerebellar involvement. The patient was unable to stand on either foot alone and exhibted some dyssynergia in both arms. There were certain endocrine features of importance, such as a senile facies, blunt, square phalanges, pigmentation of the skin and hypertrichosis. The mentality was much reduced.

Roentgenograms: The skull showed prominent convolutional markings, slight separation of the sutures and erosion of the posterior clinoid processes. The sella turcica was enlarged and encroached on the sphenoid sinus; measurements were 19 by 11 mm.

The ventriculograms showed the lateral ventricles to be greatly dilated and symmetrical. The third ventricle was dilated and was neither shifted nor encroached on. The superior portion of the aqueduct of Sylvius was greatly dilated and cone-shaped, with the apex pointing downward. The inferior portions of the aqueduct and fourth ventricle were not visualized.

Operation.—On April 3, 1930, a suboccipital craniectomy was performed. No tumor was found, but a probe inserted toward the fourth ventricle encountered

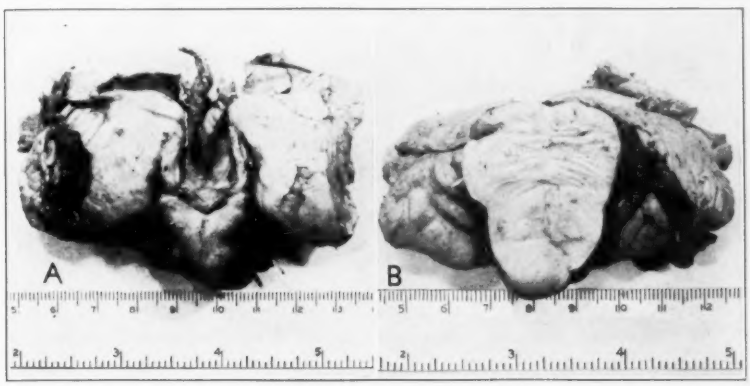

Fig. 3 (case 2).—*A*, roof of the mesencephalon viewed from above, showing enlargement of the right inferior colliculus and, to a lesser degree, of the right superior colliculus; *B*, cross-section through the mesencephalon showing the enlargement of the right inferior colliculus, due to invasion by the tumor.

obstruction at about 2.5 cm. from the cisterna magna. The patient survived the operation for two days and died with rapidly increasing hyperthermia.

Necropsy.—A small infiltrating tumor invaded the right inferior colliculus and extended across the midline to involve about one third of the left superior colliculus as well (fig. 3). The periaqueductal gray matter was greatly thickened. There was involvement of the nucleus of the third nerve. The iter was obliterated, with resulting dilatation of the third and lateral ventricles. There was invasion of the middle cerebellar peduncle. The tumor was gelatinous, and histologic examination proved it to be an astrocytoma. The following structures were not invaded by the neoplasm: the lateral geniculate body, temporal and occipital lobes, posterior commissure, inferior colliculi, internal geniculate body, lateral lemniscus, nucleus of the eighth nerve, red nucleus and superior cerebellar peduncle.

CASE 3.—*Signs of increased intracranial pressure for two years. Generalized convulsions. Pallor of disks; hyperreflexia on the right side. Enlargement of the*

sella turcica. Tumor invading the thalamus and roof of the midbrain, compressing the iter and partly filling the third ventricle.

History.—R. S., a boy aged 19, entered the University Hospital on Sept. 29, 1922, with the history that beginning two years before he had had severe attacks of vomiting, which had decreased in number. Headaches had developed six months before entrance and had increased in severity. He had had three generalized convulsions lasting one-half hour and, in addition, attacks of muscular twitching and weakness in which he fell to the left side. There was no history of diplopia, hemianopia, tinnitus or loss of hearing. Short nystagmoid movements were present on lateral fixation to the left.

Examination.—There were few signs. The pupillary reflexes and extra-ocular movements were normal. Short jerky nystagmus was present when the patient looked to the left. The visual fields were contracted, but the pupils were of normal size. The visual acuity was not recorded. The margins of the disks were fuzzy, showing marked pallor in the deeper layers. There was no papilledema. The corneal reflex on the right side was diminished. Hearing was grossly normal. The tendon reflexes on the right side were more active than those on the left, but there were no pathologic reflexes. There were no signs of cerebellar involvement.

Roentgenograms: The skull showed prominent convolutional markings. The pituitary fossa was greatly enlarged, measuring 29 mm. anteroposteriorly and 17 mm. in depth.

Operation.—A transfrontal craniotomy on the right side was performed, but no tumor was demonstrated. The postoperative course was stormy; convulsions of the left side developed, and the patient died.

Necropsy.—A tumor arising in the posterior part of the thalamus invaded the collicular region, compressed the iter and filled the posterior part of the third ventricle. As the specimen was not available for examination no further details can be given.

The difficulties in diagnosis of tumors in the tectal part of the mesencephalon are amply illustrated by these three cases. In case 1 the tumor occupied the roof of the mesencephalon, blocking the iter and producing general signs of increased intracranial pressure. Yet there were few signs of localizing significance. The sluggish reaction of the pupils and the partial homonymous hemianopia, while in themselves important, hardly point to involvement of the roof of the mesencephalon in attempts to establish a localization. In case 2 the situation was similar. There were signs of increased intracranial pressure with right homonymous hemianopia, signs of cerebellar involvement and endocrine disturbances. The total clinical impression, however, was not cleancut, so that a diagnosis was established only by means of a ventriculogram. There were even fewer signs in case 3, the syndrome in that case including increased pressure, pallor of the disks and hyperreflexia on the right side. Certainly none of these signs pointed to involvement of the roof of the mesencephalon.

Taken as a group, therefore, these cases were characterized by no signs which made a clinical diagnosis possible. Rather were they featured

by indeterminate signs, so that diagnosis was possible only by means of injections of air.

Group 2: Cases of Glioma Involving the Tectum, Tegmentum and Basis Mesencephali.—In some instances the tumors invading the mesencephalon extend farther than the tectum, giving rise to more signs than were present in the cases in group 1. A few involve both the tectum and the tegmentum of the mesencephalon, and still others invade the entire mesencephalon, occupying the tectum, the tegmentum and the basis mesencephali. The following cases illustrate the clinical picture in cases of involvement of both the tectum and the tegmentum.

CASE 4.—*Failing vision for three months, followed by dizziness. Dilatation and sluggishness of pupils, marked signs of cerebellar involvement, mild loss of motor power in the legs. Postpapillitic atrophy bilaterally. Tumor of the midline disclosed by ventriculogram. Operation without disclosure of the tumor. Glioma invading the entire region of the corpora quadrigemina, surrounding the iter, extensively invading in the tegmentum of the mesencephalon and extending into the tegmentum of the pons.*

History.—D. D., a girl aged 8, entered the University Hospital on June 4, 1931, with the history that she had had failing vision for three months; the mother had noted that the child held a book close to her face. It was also observed that the gait was unsteady. A few days later vertigo and inability to read were noted; these disturbances were followed by high fever, which was somewhat relieved by bilateral myringotomy. Unconsciousness ensued, followed by incontinence and trembling of the limbs. Both incontinence and trembling of the hands persisted. The child was unable to hold objects in her hands because of the tremors. There was no diplopia, hemianopia, tinnitus or loss of hearing.

Examination.—The pupils were dilated and did not react to light or in accommodation or convergence, and there was well marked postpapillitic atrophy. A watch was heard at 15 inches (38 cm.) from each ear. Signs of cerebellar involvement were marked, with dyssynergia in both arms, marked ataxia with falling to each side and backward and moderate dysmetria in the arms and legs as disclosed by precision tests. There was moderately diminished power in both legs, but this was not marked. The patellar and achilles tendon reflexes were more active on the right side than on the left. There were ankle clonus and a Babinski sign on the right and a questionable Babinski sign on the left side. There were no sensory disturbances. Extra-ocular movements were normal, and there was no nystagmus.

Roentgenograms: Convolutional markings were prominent, and the sutures were widely separated. The posterior clinoid processes were eroded; the sella turcica was enlarged and encroached on, almost obliterating the sphenoid sinus.

In the ventriculograms, the third ventricle and lateral ventricles were seen to be enormously dilated. They were not encroached on or displaced. The aqueduct of Sylvius and the fourth ventricle were not visualized.

Operation.—A suboccipital craniectomy was performed on June 16, 1931. No tumor was disclosed in the vermis of the cerebellum. Fluid could be seen flowing from the aqueduct. A small cystic cavity was disclosed close to the midline, and this was thought to be part of the tumor. The patient did well after the operation, but on the morning of the third day the pulse rate rose to 200, convulsions and hyperthermia developed and the patient died despite all efforts to save her.

Necropsy.—There was internal hydrocephalus. A large glioma involved the entire region of the corpora quadrigemina and surrounded the iter (fig. 4). The tumor was largely in the tegmentum, involving the lateral lemniscus and the superior cerebellar peduncle. The tectum of the pons was invaded as far as the level of the nucleus of the trigeminal nerve. The right pulvinar thalami was invaded by the tumor. The anterior part of the fourth ventricle was occluded, but the remainder was free. Histologic examination showed that the tumor was an astrocytoma. There was no involvement of the lateral geniculate body, the temporal or occipital lobe, the medial geniculate body, the nucleus of the eighth nerve, the red nucleus or the posterior commissure.

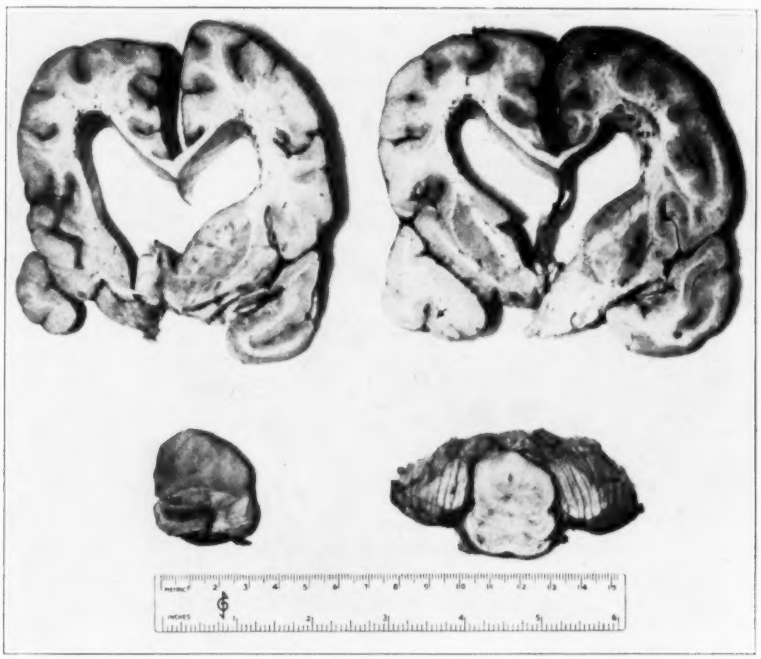

Fig. 4 (case 4).—Section of the brain showing a tumor involving the roof of the midbrain. Note the extreme hydrocephalus.

In this case there were many more signs than in those in group 1. The dilatation and sluggishness of the pupils are of doubtful value when associated with postpapillitic atrophy of this degree. The signs of cerebellar involvement were due undoubtedly to invasion of the superior cerebellar peduncle, and the weakness of the legs may be ascribed to involvement of the pyramidal fibers.

The signs of cerebellar involvement were the outstanding features and might have directed attention to the posterior fossa, but the presence of weakness in the legs should suggest a lesion occurring in an area

where cerebellar and motor fibers lie close together—either the pons or the mesencephalon. The absence of palsies of the cranial nerves would contraindicate a diagnosis of pontile tumor. The additional presence of marked sluggishness of the pupils should suggest a mesencephalic localization, but the value of these pupillary signs in the diagnosis of tumor will probably be challenged. Their significance will be discussed subsequently.

CASE 5.—*Difficulty in speech; tremors of the right hand; shaking of the right foot. Papilledema, right hemiparesis; moderate signs of cerebellar involvement. Right homonymous upper quadrantanopia. Tumor invading the left side of the midbrain and pons.*

History.—M. L., a girl aged 6 years, entered the University Hospital on May 8, 1934. About eight months before the parents noted slowness in the child's speech; this was followed a month later by intention tremors of the right hand and jerking movements of the right leg and foot. A month before the patient entered the hospital signs of increased intracranial pressure appeared.

Examination.—There were bilateral choked disk of 3 or 4 diopters and right homonymous upper quadrantanopia. Slight paresis and a positive Babinski sign were present on the right side. Hypermetria was present in the right arm and leg; the gait was unsteady, and there was some unsteadiness when the patient was tested for evidence of the Romberg sign. Sensation was everywhere normal. Convergence was poor; otherwise the extra-ocular movements were normal. The pupils were of average size, and the pupillary responses were normal in all phases. There was nystagmus. Hearing was normal.

Roentgenograms: Convolutional markings were visible on the inner table, and the sutures were widened. The sella turcica was normal.

Ventriculograms showed that the lateral ventricles were dilated and symmetrical. The third ventricle was also dilated, and there was a filling defect in the posterior inferior portion. The aqueduct and the fourth ventricle were not visualized (fig. 5).

Operation.—On May 1, 1934, a suboccipital craniectomy was performed, but no tumor was exposed. The patient died three days later without regaining consciousness.

Necropsy.—A glioma involved almost the entire left side of the midbrain, pushing the iter upward and occluding the posterior end of the third ventricle (fig. 6). There was invasion of the superior and inferior colliculi. The only structures spared in the mesencephalon were the lateral lemniscus, the medial geniculate body and the periaqueductal gray matter. The reticular tissue, nucleus ruber and substantia nigra were invaded by the tumor. The tegmentum of the pons was involved, the tumor extending only to the anterior half of the pons. Histologic examination showed that the tumor was an astrocytoma.

In this case, despite the greater number of signs, it was not easy to make a diagnosis. There were obviously increased intracranial pressure with mild paresis and signs of cerebellar involvement on the right side and a history of involuntary movements of the right arm. In this case, too, as in the preceding one, the presence of both motor disturbances and signs of cerebellar involvement should suggest a lesion either in the mesencephalon or in the pons, despite the absence of signs of involve-

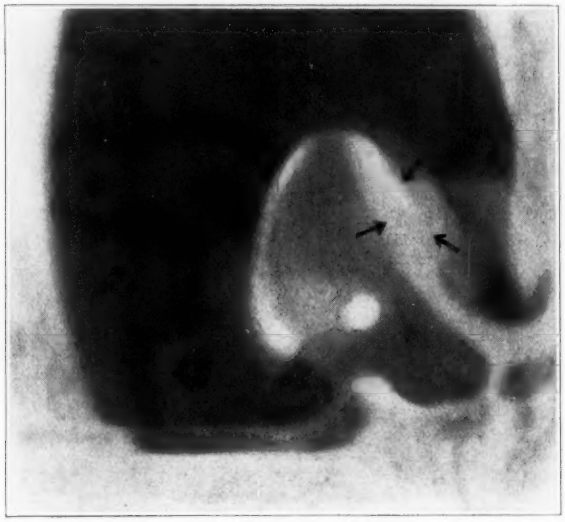

Fig. 5 (case 5).—Drawing of a ventriculogram, lateral view, taken when the patient was lying face down. The arrows indicate a filling defect in the floor of the posterior part of the third ventricle.

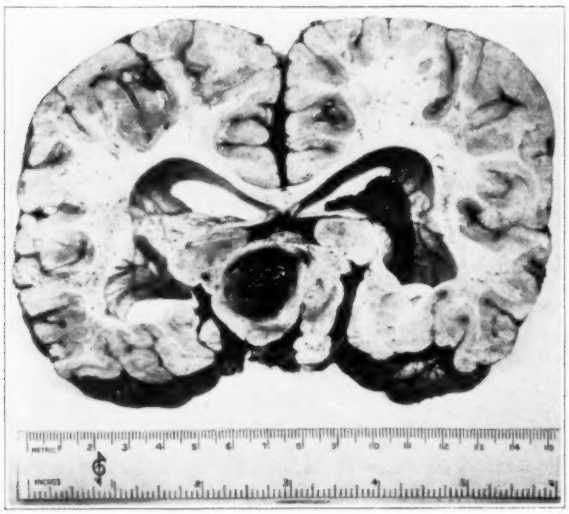

Fig. 6 (case 5).—Section of the brain showing a large tumor filled with hemorrhage in the left side of the mesencephalon destroying most of the tectum and some of the basis mesencephali.

ment of the cranial nerves. The hemiparesis was due to invasion of the peduncle. The tremors of the right arm were due possibly to involvement of the left nucleus ruber, and the signs of cerebellar involvement, manifested on the right side, to invasion of the right superior cerebellar peduncle.

CASE 6.—*Weakness of the left arm and leg; failing vision; nystagmus; diplopia; unilateral stiffness of the pupil; paralysis of upward ocular movements; bilateral impairment of hearing; weakness of the left side of the face and left leg; signs of cerebellar involvement on the left side. Suggestion of superior bitemporal hemianopia. Encephalogram suggestive of tumor of the midline near the aqueduct. Glioma invading the diencephalon, mesencephalon and pons.*

History.—D. B., a man aged 51, entered the University Hospital on Nov. 12, 1930, complaining of generalized weakness, more marked on the left side. Fourteen months previously he had noticed that he tired easily and experienced a general lack of strength. This was followed by swelling of the face, which was relieved by drainage of the maxillary antrums. Later on he noticed that he bumped into objects on his left side. The left arm and leg became weak two months before entrance, and a month later he noticed slight impairment of vision and diplopia. No history of tinnitus, unsteadiness of gait, involuntary movements or convulsions was obtained. Although the patient did not complain of loss of hearing, it was evident to one taking the history that he was deaf.

Examination.—There was a combination of signs indicating involvement of cranial nerves and of the cerebellum and motor disturbances. There was rotatory nystagmus when the patient attempted to gaze upward and diplopia when he looked to the right. There were paralysis of upward ocular movements and paralysis of the right internal rectus muscle. The nasal sides of both optic disks were pale, but there was no papilledema. The right pupil was dilated—it measured 4 mm. and the left measured 2 mm.—and was fixed to light and in consensual and convergence reactions. Vision was greatly impaired, the patient being barely able to read large head-lines in the newspaper. There was a suggestive superior bitemporal quadrantanopia, especially when a red test object was employed. Acuity of hearing was impaired bilaterally, but the impairment was more marked on the left side. The patient could hear a watch tick at a distance of 1 inch (2.54 cm.) from the right ear but could not hear the watch even when it was in contact with the left ear. The left leg was weak, and there was weakness of the left corner of the mouth but none of the left arm. The gait was unsteady, and the patient walked with a wide base, often falling to the left. There were hypometria of the left arm and leg and slight dyssynergia of the left arm. The patellar reflexes were slightly increased on the left side.

Roentgenograms: The sella turcica was normal; there were no convolutional markings and no separation of the sutures. The lateral ventricles were slightly dilated and symmetrical. The third ventricle was slightly dilated but presented a filling defect in the inferior portion, the defect being greater posteriorly. The aqueduct of Sylvius and the fourth ventricle were clearly visualized. They appeared displaced slightly posteriorly, but by measurement they were only 3.7 mm. from the dorsum sellae.

No operation was performed; the patient left the hospital and died at home, two and one half months later.

Necropsy.—A tumor was invading the diencephalon, mesencephalon and pons. It involved the left thalamus, internal capsule and hypothalamic region, occluding

the third ventricle (fig. 7). It occupied practically the entire left side of the mesencephalon, the lateral geniculate body and superior colliculus on the left, and the cerebral and cerebellar peduncles, red nucleus, lateral lemniscus and nucleus of the third nerve bilaterally. In the posterior portion of the mesencephalon it invaded the right side. It involved the left side of the pons. Histologic examina-

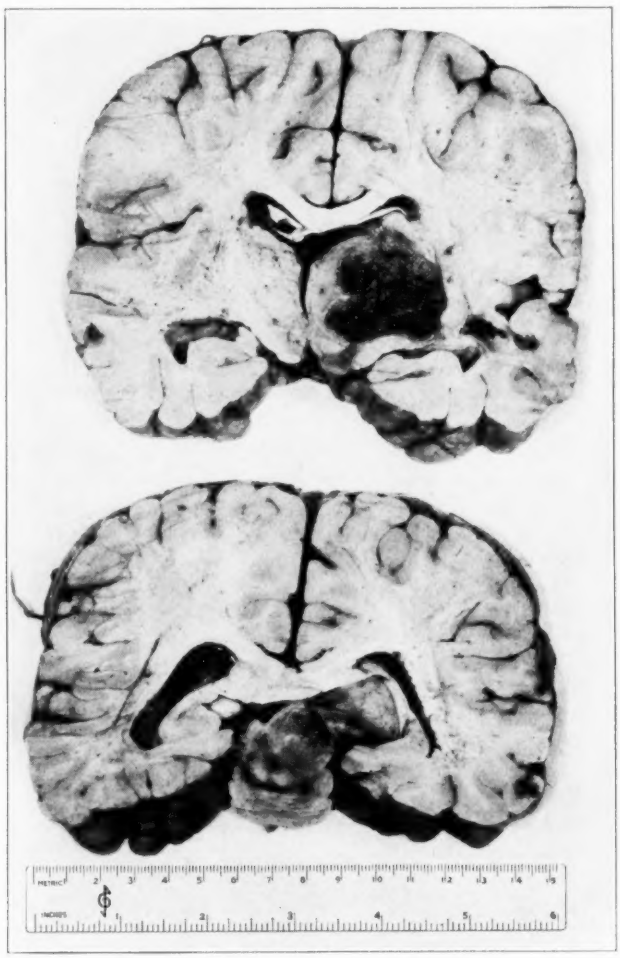

Fig. 7 (case 6).—Section of the brain showing a large infiltrating glioma involving the right side of the diencephalon and mesencephalon.

tion showed that the tumor was an astrocytoma. The nucleus of the eighth nerve was spared; the inferior colliculi and medial geniculate bodies and the posterior commissure were not available for examination.

The diagnosis in this case was not difficult because of the abundance of signs, many of which pointed to involvement of the mesencephalon.

The oculomotor paralysis and the paralysis of upward ocular movements were important signs, and these, together with the combined motor disturbances and signs of involvement of the cerebellum indicated the localization of the tumor. The hemianopia in this case is worthy of mention; it may have been due to involvement of the lateral geniculate body. The unilateral stiffness of the pupil to all forms of stimulation is of interest. The bilateral loss of hearing was probably due to invasion of both lateral fillets.

CASE 7.—*Dizziness and loss of consciousness; sluggishness of the pupils; right ophthalmoplegia; bilateral palsy of the external rectus muscle; left hemiparesis, hyperesthesia of the left arm and leg; astereognosis in the left hand; bilateral signs of cerebellar involvement; left homonymous defect in the fields. Glioma of the mesencephalon and pons.*

History.—O. F., a man aged 53, entered the University Hospital on Feb. 25, 1931, with the complaint of dizziness and inability to walk well. Five months before he had fallen on his back and remained unconscious for thirty minutes. Three months later he had frequent spells of dizziness and walked with a staggering gait. He fell frequently and lost consciousness. He observed that he walked as if he were drunk. The patient did not complain of diplopia, hemianopia, tinnitus, loss of hearing or convulsions.

Examination.—The right pupil reacted sluggishly to light. Visual acuity was 6/15 in the right eye and 6/12 in the left. A left homonymous defect was found on examination of the visual fields. There was no papilledema or pallor of the disks. There was complete ophthalmoplegia of the right eye, except for a slight movement upward. The left trigeminal nerve was involved in both the motor and the sensory portion. Bilateral palsy of the abducens nerve was present. Nystagmus was not observed. Hearing was normal in both ears. There was paresis, not involving the face, on the left side. There were bilateral signs of cerebellar involvement, with dyssynergia in both arms and inability to stand or sit. There was considerable dyssynergia in the trunk. There were hyperesthesia of the left arm and leg, loss of sense of position in the left big toe and astereognosis in the left hand. Mentally, there were marked jocularity and unreliability in responses.

Roentgenograms: The calvarium was normal, showing no convolutional markings or separation of the sutures. The sella turcica was top-normal in size.

An encephalogram showed normal cortical markings but no filling of the third ventricle or of the lateral ventricles. The fourth ventricle was clearly seen; it was normal in size but appeared displaced posteriorly. The distance from the dorsum sellae to the base of the fourth ventricle was 4.2 cm.

Operation.—On March 12, 1931, several trephine openings were made for the exposure of a possible subdural hematoma. None was disclosed. Death ensued in three days.

Necropsy.—A large glioma invaded the right side of the mesencephalon, involving the lateral geniculate body, nucleus ruber, superior cerebellar peduncle, superior colliculus, cerebral peduncle, lateral lemniscus and medial geniculate body. The tumor extended backward into the tegmentum of the pons, where it involved the right middle cerebellar peduncle and the right cerebellar hemisphere. The tumor invaded the sheath of the right oculomotor nerve but not the periaqueductal gray matter at the nucleus of the third nerve.

Histologic examination showed that the tumor was a glioblastoma multiforme.

The combination of signs of involvement of cranial nerves, and of the cerebellum and motor and sensory disturbances indicated a lesion in the mesencephalon and pons; hence localization was not difficult in this case. Of particular interest is the ophthalmoplegia on the right side, which was produced by a small tumor nodule invading the sheath of the right oculomotor nerve.

CASE 8.—*Symptoms of increased pressure; papilledema; right inferior homonymous defect in the fields; right hemiparesis; signs of cerebellar involvement. Glioma of the mesencephalon and pons.*

History.—H. S., a boy aged 16, entered the University Hospital on Sept. 11, 1930, with the history that he had had severe, throbbing headaches for four months. For two months he had been vomiting and had had "blind flashes," during which he became blind for a few seconds. For two weeks he had been troubled with diplopia. There was no history of staggering gait, loss of hearing, hemianopia, involuntary movements or convulsions.

Examination.—The disks were choked—4 diopters in the left and 6 diopters in the right eye; vision was 6/6 in the right eye and 6/12 in the left. The pupillary reactions were normal. There was a right homonymous defect in the fields. Nystagmus was present when the patient looked upward and to either side. Hearing was normal in both ears. The tongue protruded slightly to the left. There were no other signs at the time of examination.

Roëntgenograms: There was evidence of increased intracranial pressure from the convolutional markings on the skull and from the enlarged sella.

There was dilatation of the third ventricle and of both lateral ventricles. The anterior part of the third ventricle was well filled with air and could be seen extending into the sella turcica. There was a filling defect in the posterior part of the third ventricle, and neither the iter nor the fourth ventricle was visualized. The third ventricle was displaced slightly to the right, and the medial aspect of the posterior and inferior horns of the left lateral ventricle showed a filling defect.

Operation.—On Sept. 23, 1930, a suboccipital craniectomy was performed, and the right cerebellar hemisphere was found to be larger than the left. The patient was discharged somewhat improved.

Second Admission.—The patient was readmitted on Nov. 20, 1930, complaining of loss of hearing in both ears, failing vision and difficulty in walking. Examination at this time revealed only 3 diopters of choking in each eye, nystagmus on lateral deviation to the left, right inferior homonymous quadrantanopia and a diminution in acuity of hearing in both ears. At this time there were right hemiparesis, positive Romberg sign, incoordination of the legs, and dyssynergia and dysmetria in the arms and legs. Sensation was normal.

An operation was performed on Dec. 16, 1930, and a tumor of the third ventricle was partially removed by the transcallosal route. The patient reacted poorly and died with hyperthermia a few days later.

Necropsy.—A glioma involved the left thalamus, chiefly the pulvinar, and the left medial and lateral geniculate bodies. It extended into the mesencephalon and pons, where it invaded the superior and inferior colliculi and the entire aqueductal gray matter. Histologically, the tumor was an astroblastoma. There was no invasion by neoplasm of the lateral lemniscus, red nucleus, superior or cerebellar peduncle, nucleus of the eighth nerve or posterior commissure.

The diagnosis on the patient's first admission was obscure, but after the second admission the signs conformed to those occurring in cases of mesencephalic tumors of an extensive type, such as were seen in the preceding two cases. The loss of hearing was probably due to damage of the left medial geniculate body, though it was bilateral. Homonymous quadrantanopia was associated with invasion of the lateral geniculate body and the superior colliculus.

Syndrome Simulating Occlusion of the Superior Cerebellar Artery: In two cases the clinical syndrome simulated that observed in cases of occlusion of the superior cerebellar artery.

CASE 9.—*Numbness of the left side of the body; pain in the left arm and leg. Signs of increased intracranial pressure; involuntary movement of the right arm and leg; fixed, unequal pupils; flaccid left hemiplegia and left hemianesthesia. Evacuation of cyst. Glioma of the right side of the midbrain.*

History.—E. S., a man aged 27, was brought to the University Hospital on June 28, 1934, after he had become stuporous a few hours previously. Four months before he had noted numbness of the left foot, extending up the leg and eventually, after several weeks, involving the entire left side of the body. For two months he had been limping with the left leg, and for one month he had had severe pain in the left arm and leg. Vision had been failing for two months, and within the last weeks before admission signs of increased intracranial pressure had developed. There was no history of diplopia, hemianopia, tinnitus or loss of hearing.

Examination.—There were purposeless, involuntary movements of the right arm and leg and a flaccid hemiplegia of the left side. There was hemianesthesia to pinprick over the entire left side of the body. The pupils were fixed to light, both in direct and in consensual reactions, but reacted in accommodation; they were regular, but the right pupil was larger than the left. There were no other neurologic signs. Visual fields, associated movements of the eyes and hearing could not be tested. No choking of the disks was present.

Roentgenograms: No convolutional markings were visible, nor were the sutures widened. The sella turcica was normal. The lateral ventricles were moderately dilated. The third ventricle was faintly visualized in the lateral view and appeared as a thin line with its convexity to the left in the anteroposterior view. The aqueduct and the fourth ventricle were not visualized.

Operation.—On June 29, 1934, a right temporoparietal exploration was made and a cyst evacuated through the second temporal convolution. The contents consisted of a straw-colored fluid which coagulated on standing. The patient stood the operation poorly and died four days afterward.

Necropsy.—A glioma invaded the right side of the diencephalon and mesencephalon. It involved the posterior part of the thalamus, the posterior limb of the internal capsule, the lateral geniculate body, the nucleus ruber, the superior colliculus and to a slight degree the nucleus of the third nerve. The superior cerebellar peduncle was spared. The tumor involved, therefore, practically the entire right side of the diencephalon and mesencephalon. Histologic examination proved that the tumor was an astroblastoma.

This case is of particular interest from the diagnostic standpoint, for the presence of hemiplegia and hemianesthesia with fixed pupils and involuntary movements of the opposite side of the body suggests a syn-

drome referable to the midbrain similar to that occurring in cases of occlusion of the superior cerebellar artery, except for the pupillary signs. In fact, a diagnosis of such a syndrome was made clinically, though it was made clear that it was probably due to a tumor rather than to vascular disease. The site of the glioma explains all the signs, the involuntary movement possibly being due to involvement of the nucleus ruber.

CASE 10.—*Vomiting; pain in the abdomen; headache; staggering gait; diplopia; numbness of the right arm and leg; signs of cerebellar involvement; normal fundi; paresis and hypesthesia on the right side. Posterior displacement of the aqueduct and fourth ventricle shown by encephalogram.*

History.—M. S., a girl aged 13, entered the University Hospital on April 25, 1934, with a complaint of vomiting, pain in the abdomen and headache which

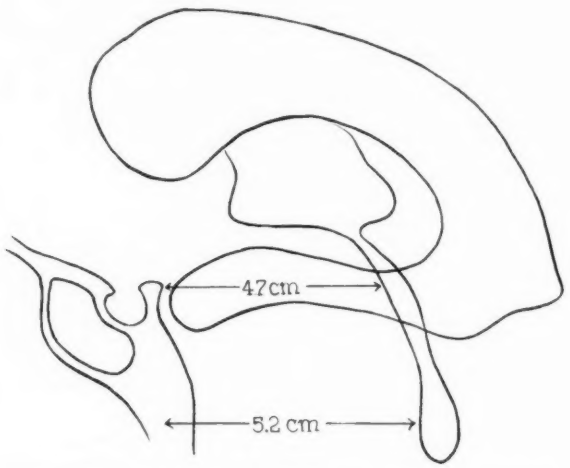

Fig. 8 (case 10).—Sketch of a ventriculogram showing posterior displacement of the aqueduct of Sylvius and fourth ventricle by a mesencephalic tumor. The distance between the dorsum sellae and the base of the fourth ventricle varies from 3.3 to 4 cm. in normal subjects.

began suddenly on Dec. 23, 1933. Five days later the mother noted that the patient exhibited unsteadiness of gait. A month after the onset, after an attack of vomiting, diplopia developed, and the mother observed an internal squint of the left eye. In March 1934 there developed weakness and numbness of the right leg and inability to write with the right hand.

Examination.—The visual fields were normal; the acuity of vision was good, and the fundi were normal. There was paralysis of the left abducens nerve. Signs of cerebellar involvement, such as dyssynergia, dysmetria and dysdiadokokinesis, were prominent in the right arm and leg. Nystagmus was present when the patient looked to the right or left. A slight weakness of the right side was present, with diminished sense of pain, touch and stereognosis. An audiogram showed an 18.1 per cent loss of hearing in the right ear and 17 per cent in the left ear.

Roentgenograms: There was no evidence of increased intracranial pressure. Ventriculograms showed moderately dilated third and lateral ventricles, which were neither displaced nor encroached on. There was definite posterior displacement of the aqueduct of Sylvius and the fourth ventricle. The distance from the dorsum sellae to the aqueduct was 4.7 cm., and that from the dorsum sellae to the base of the fourth ventricle was 5.2 cm. (fig. 8).

A diagnosis of mesencephalic glioma was made, and this was confirmed by the ventriculogram.

Course.—Roentgen therapy was administered and was followed by improvement. The patient was readmitted to the hospital on June 27, 1934, because of a recurrence of headache, vomiting, diplopia, weakness of the right arm and leg and drowsiness. Roentgen therapy again brought about improvement within a few days. When the patient was last seen, on Oct. 13, 1934, the only complaint was diplopia, due to a complete palsy of the left abducens nerve, which has persisted.

In this case, too, the signs were those of occlusion of the superior cerebellar artery, with weakness, sensory disturbances and signs of cerebellar involvement on the right side. The involuntary movements commonly associated with this syndrome were lacking, but the other signs conformed to those frequently observed in cases of involvement of the superior cerebellar artery.

SYNDROMES OF MESENCEPHALIC TUMORS

The preceding examples demonstrate amply some of the difficulties in the diagnosis of mesencephalic tumors. These tumors may be grouped roughly into the tectal and the tectal-tegmental-basal group.

Tectal Group.—There were three cases of tectal tumor in this series, in all of which there was clinical and roentgen evidence of increased intracranial pressure. No localizing signs were present. In the presence of increased intracranial pressure, when there are obscure pupillary or oculomotor signs it is necessary to be on guard against the possibility of a tumor in the roof of the mesencephalon. When a tumor does not invade the periaqueductal gray matter even the pupillary changes may be absent. The only means of diagnosis is injection of air. In none of the three cases of tumor of the tectum, for example, was there anything which would enable one to diagnose the localization. In only one case were there pupillary signs, and these were such as to make their significance doubtful in the diagnosis of tumor. A partial homonymous hemianopia was present in two cases. All three patients had a history of generalized convulsions, but since no convulsive seizures were observed in the hospital it is not known whether those mentioned in the history were tonic or clonic.

It is clear, therefore, that the diagnosis of a tumor involving the tectum mesencephali is at best uncertain, and in the present state of knowledge of the function of this region, it must depend on the injection of air.

Tectal-Tegmental-Basal Group.—In cases in which the tumor invades more than the roof of the mesencephalon the signs are much more clear-cut. The number of signs are roughly proportionate to the amount of tissue invaded.

In the three cases of tumor involving the tectum and tegmentum, one finds a variety of syndromes. In case 4, for example, there was a combination of pupillary and motor disturbances and signs of cerebellar involvement which suggest a mesencephalic lesion. In case 5, the involuntary tremors, the hemiparesis and the signs of cerebellar involvement are similarly suggestive. In all these cases the outstanding characteristic is the combination of motor disturbances and signs of cerebellar involvement with some involvement of the cranial nerves. The latter, however, is not so constant because in this group of cases the invasion of the tegmentum is much more pronounced than that of other portions of the mesencephalon.

When the entire mesencephalon—tectum, tegmentum and basis—is invaded by a neoplasm, the diagnosis is easy. In such cases there is a combination of signs of involvement of cranial nerves and of the cerebellum and motor disturbances. There is often extension into the pons, with involvement of the cranial nerves from the third to the seventh pair. Usually, signs of cerebellar involvement are pronounced. Motor disturbances are usually definite but may not be marked. Sensory changes are not a prominent feature, as a rule.

PATHOLOGIC OBSERVATIONS

All the tumors in this series were gliomas. All were infiltrating tumors, poorly defined and not enucleable. All were solid except one, which was partly cystic, the contents of the cyst being thick and gelatinous. In three cases the tumor was confined entirely to the mesencephalic roof (cases 1 to 3). All these tumors were small, one of them (case 2) being confined entirely to the region of the posterior commissure, another (case 1) to the inferior colliculus and the third (case 3) to the collicular region and the adjacent thalamus. In two cases (4 and 6) the tumor involved the mesencephalon and the adjacent diencephalon. In one instance (case 5) the tumor was confined entirely to the mesencephalon. In the other cases (8, 9 and 10) the growth had extended into the diencephalon, mesencephalon and pons, the bulk of the tumor being located in the first two structures. While the greater part of the glioma is confined to one side, it is not unusual to find that it has extended across the midline to a greater or lesser degree. There seems to be a predilection on the part of the glioma to invade the tectal portions of the mesencephalon, but the other parts were by no means spared and may be extensively invaded. The neoplasm appears to be confined almost

entirely to the base of the brain, but there are exceptions even to this rule, for in case 8 the tumor extended into the posterior horn of the ventricle.

There is no uniformity in the histologic picture exhibited by mesencephalic gliomas. Four of the ten in this series were astrocytomas, two were astroblastomas and one was a glioblastoma multiforme. Three were not studied histologically.

COMMENT ON SPECIAL SIGNS IN CASES OF MESENCEPHALIC TUMOR

The Pupils.—The problem arises whether pupillary signs may be of diagnostic value, especially in cases of tumor involving the tectum and periaqueductal gray matter. In five of the nine fatal cases there were changes in the pupils of various sorts. In only one instance was there a typical Argyll Robertson pupil. In this case (case 9) both pupils were fixed to light, were miotic and unequal and reacted in accommodation. The reactions to homatropine and to painful stimuli were not tested. The collicular region, particularly on the right side, was invaded by the tumor. The tumor also extended into the nucleus of the right oculomotor nerve. This is the only case in which there was an Argyll Robertson pupil.

The diagnostic value of such pupils in cases of mesencephalic tumor has been discussed by Wilson and Rudolf [1] and by Wilson and Gerstle,[2] who provided evidence that an infiltrating tumor involving the anterior colliculi may produce the Argyll Robertson sign. Two such cases with necropsy were recorded by Wilson and Gerstle. While it is true that in practically all instances an Argyll Robertson pupil is pathognomonic of syphilis, there is no doubt that in rare instances similar pupillary changes may be produced by an invading mesencephalic tumor and that in these instances the involvement may be unilateral or bilateral.

The number of instances in which typical Argyll Robertson pupils occur in cases of mesencephalic tumor is small. A careful analysis of our records was made to determine whether pupillary changes of other sorts may indicate a mesencephalic tumor. In three cases the pupils reacted sluggishly to light. In one of these cases there was marked atrophy of the disks; so this reaction loses its significance. In the other instance, the sluggishness of the pupil was part of a complete ophthalmoplegia. In the third case the pupils reacted sluggishly to light, but this in itself could hardly be looked on as significant. Sluggish pupils per se,

1. Wilson, S. A. K., and Rudolf, G. de M.: Case of Mesencephalic Tumor with Double Argyll Robertson Pupil, J. Neurol. & Psychopath. **3**:140, 1922.

2. Wilson, S. A. K., and Gerstle, M.: The Argyll Robertson Sign in Mesencephalic Tumors, Arch. Neurol. & Psychiat. **22**:9 (July) 1929.

therefore, cannot be considered to be of value in the localization of the tumors with which we are concerned.

In one instance only one pupil was fixed to light and in accommodation; it did not show a typical Argyll Robertson reaction. This pupillary reaction was part of a complete ophthalmoplegia on the right side.

In cases of mesencephalic tumors, therefore, unilateral or bilateral Argyll Robertson pupil is of great localizing value; failure of the pupil to react to light or in accommodation, whether unilaterally or bilaterally, is likewise a valuable diagnostic criterion but is usually found in combination with evidences of external ophthalmoplegia. Sluggishness of the pupil is of itself of no import.

Other Ocular Signs.—In two instances there was unilateral ophthalmoplegia, in one complete and in the other incomplete. Ophthalmoplegia occurs in any case in which a tumor invades the oculomotor nerve or nucleus. In one of our cases it was caused by invasion of the oculomotor nerve and its sheath by the tumor; in that case the opthalmoplegia was practically complete. In another case it was caused by invasion of the oculomotor nuclei.

Visual Fields.—Partial hemianopia was present in six of our patients (one was blind and another stuporous, so that the visual fields could not be tested). The defects in the fields were not as clearcut as they frequently are in cases of perichiasmal tumor or of a neoplasm invading the temporal or occipital lobe. Not only was the macula spared in every instance, but the area of blindness rarely approached it closely. The defects in the fields were bounded, not by straight lines and angles, but by curves.

In three cases in which one lateral geniculate body was invaded by a neoplasm (cases 5, 7 and 8) a contralateral homonymous quadrantanopia was disclosed by the visual fields (fig. 9). One patient (case 7) with unilateral involvement of the lateral geniculate body had a suggestive bitemporal superior quadrantanopia, especially when a red test object was employed. In other cases a suggestive bitemporal hemianopia was present. As approximately 90 per cent of the fibers of the optic radiation enter the lateral geniculate body, these defects in the fields are readily understandable. One or both superior colliculi were also invaded by tumor tissue in cases 5, 6, 8 and 9. The tumor did not encroach on the temporal or occipital lobes.

More difficult to explain is hemianopia in two cases in which the tumor did not extend into the lateral geniculate bodies or the temporal or the occipital lobes. In case 1 there was a suggestive left homonymous hemianopia; at autopsy the left superior colliculus was seen to be greatly enlarged by the tumor. In case 2 there was a definite right homonymous hemianopia; the right superior colliculus was almost completely destroyed, and about one third of the left was invaded by the tumor.

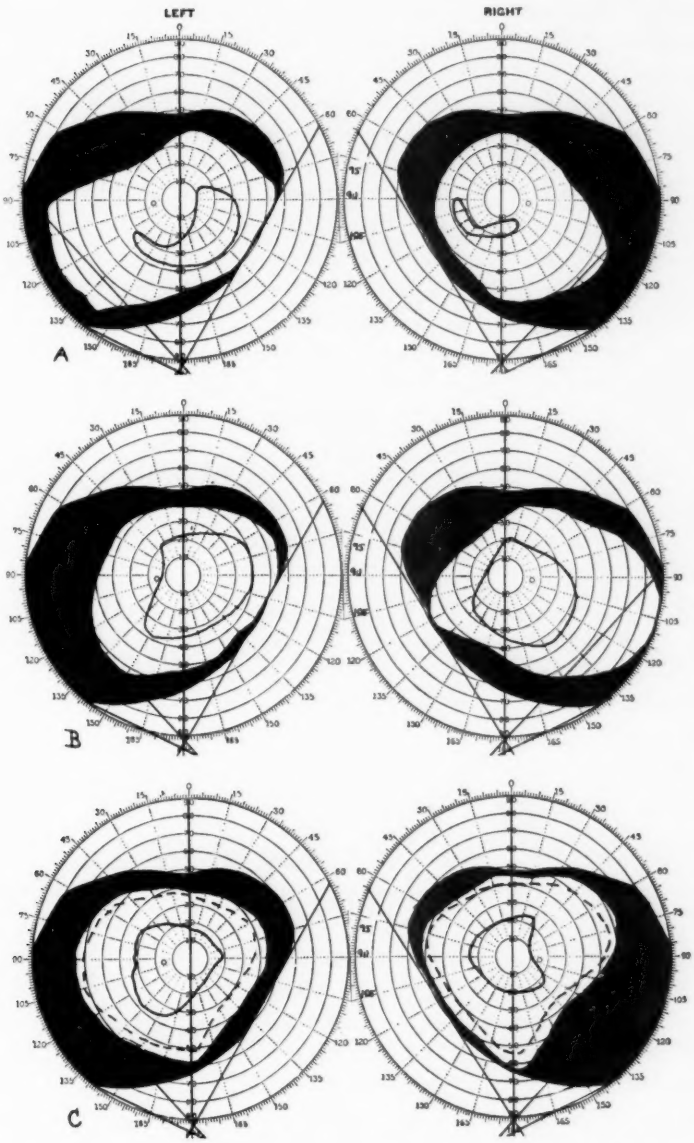

Fig. 9.—Visual fields showing: *A* (case 6) homonymous defects; *B* (case 7) homonymous defects; *C* (case 8) bitemporal defect.

Neither our material nor any statements we have found in the literature make one think that injury to the superior colliculi causes hemianopia.

Roentgenograms.—In all three cases of glioma confined to the tectum mesencephali, convolutional markings were prominent on the inner table of the skull; the sutures were separated; the posterior clinoid processes were eroded, and the sella turcica was enlarged. These are signs of long-standing increased intracranial pressure, but they are not of localizing significance. Ventriculograms, which were made in only one of the three cases, showed definite evidence of a tumor of the midbrain. The lateral and third ventricles were dilated and the superior part of the aqueduct was greatly enlarged, but the lower portion of the aqueduct and the fourth ventricle were not visualized.

Of the seven cases in which a glioma occupied the tegmentum mesencephali, with or without invasion of the basis, there was no roentgen evidence of increased intracranial pressure in five. Studies by injection of air were made in all cases. A filling defect in the posterior part of the third ventricle was present in four. In all seven cases the aqueduct of Sylvius and the fourth ventricle were displaced posteriorly or there was a failure to visualize these structures.

In the presence of dilated third and lateral ventricles with a free communication between the lateral ventricles, a filling defect in the posterior part of the third ventricle obviously indicates the location of the tumor. The diagnosis of the site of origin and type of tumor depends on the clinical history and examination. One cannot always differentiate mesencephalic glioma, pinealeoma and a benign tumor within the third ventricle by means of ventriculograms alone.

Posterior displacement of the aqueduct and fourth ventricle is diagnostic of a tumor of the midbrain or pons. An intramedullary or extramedullary tumor situated anterior to the iter may cause such a shift. Dyke and Davidoff [3] have pointed out that the distance between the dorsum sellae and the base of the fourth ventricle in encephalograms of normal brains is fairly constant, varying from 3.3 to 4 cm. If this dimension is much increased, they say, it is evidence of a tumor.

Failure to visualize the aqueduct and fourth ventricle deserves special mention. In three of the four cases in which neither the aqueduct nor the fourth ventricle was visualized, a filling defect indicated extension of the tumor into the region of the third ventricle. We believe that, with the proper technic, when the third and lateral ventricles are moderately dilated, failure to visualize the iter and fourth ventricle is strongly indicative of obstruction of the aqueduct of Sylvius.

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3. Dyke, C. G., and Davidoff, L. M.: The Demonstration of Normal Cerebral Structures by Means of Encephalography: IV. The Subarachnoid Cisterns and Their Contents, Bull. Neurol. Inst. New York **3**:418, 1934.

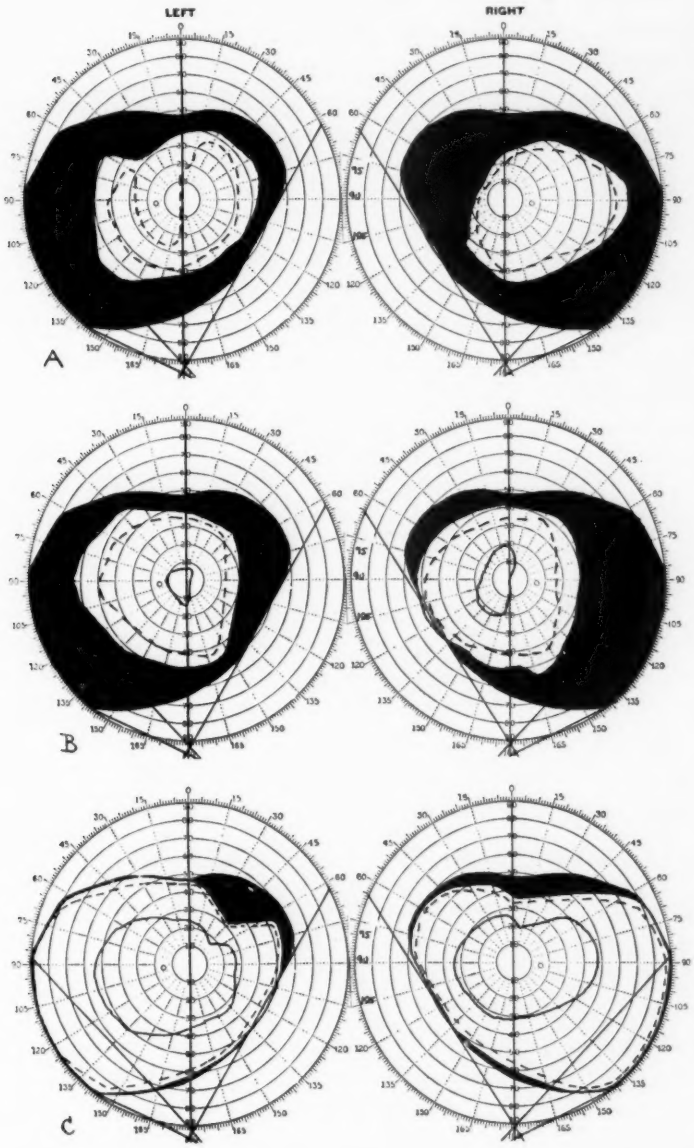

Fig. 10 (cases 1, 2 and 5).—Results of perimetric examinations showing homonymous defects in the fields. *A*, case 1; *B*, case 2; *C*, case 3.

Obstruction of the aqueduct may be the result of a primary mesencephalic tumor or of extension of a cerebellar tumor, such as an ependymoma or a medulloblastoma. A carefully taken history with consideration of structures passing through the midbrain allows one to make a differential diagnosis.

Hearing.—Our material presents little evidence concerning the auditory pathways. Tests with the audiometer were made in only one instance; hence only gross defects in hearing were detected. One patient with bilateral deafness (case 8) was found to have invasion of both lateral lemnisci by the tumor. No significance can be attached to failure to demonstrate loss of hearing in the other patients with invasion of structures thought to form a part of the auditory pathway, because the tests used were too crude to detect moderate loss of hearing.

The relation of the posterior colliculi to hearing was studied by Weinland [4] in 1894, when he described a case of unilateral loss of hearing associated with a tumor of the corpora quadrigemina and collected reports of eighteen cases from the literature. Deafness was present in nine, in three of which it was unilateral. From his own case and from those of Ferrier and Reul, Weinland concluded that damage to one posterior colliculus causes loss of hearing on the opposite side. Preservation of hearing in the other ten cases was explained by him as follows: Some patients were stuporous; the lateral lemnicus and the posterior quadrigeminal brachium may have been spared, or mild degrees of deafness may have been overlooked. After bilateral destruction of the posterior colliculi in trained dogs, Rothmann [5] found that complete deafness existed for a few days. After a long time these dogs could hear loud noises and could again be trained to some degree of discrimination, but their hearing was never like that of normal dogs.

SUMMARY

Despite the rather wide variation in the clinical pictures encountered in cases of mesencephalic glioma, it is possible to draw some practical conclusions. First, it is certain that the diagnosis of a tumor involving the tectum mesencephali is most uncertain clinically and depends in the last analysis on injection of air. In cases of more extensive glioma involving the tectum and tegmentum or the tectum, tegmentum and basis mesencephali, there is a combination of signs of involvement of

4. Weinland, E.: Ueber einige Tumore der Vierhügelgegend und über die Beziehungen der hinteren Vierhügel zu Gehörsstörungen, Arch. f. Psychiat. **26**: 363, 1894.

5. Rothmann, M.: Zur Function der hintern Vierhügel, Neurol. Centralbl. **26**:922, 1907. Ueber die Ergebnisse der Hörprüfung an dressierten Hunden, Arch. f. Anat. u. Physiol. (Physiol. Abt.), 1908, p. 103.

cranial nerves (chiefly oculomotor) and of the cerebellum and motor and sensory disturbances. Occasionally a syndrome simulating that of occlusion of the superior cerebellar artery is encountered. Choked disk may be present, though almost as frequently it is absent, and subjective signs of increased pressure are often pronounced. In rare instances a pupil simulating the Argyll Robertson pupil may be encountered. It should be emphasized, however, that the pupillary reactions are not those of the typical Argyll Robertson pupil, for there is loss of response both to light and in accommodation and sometimes even to consensual stimulation.

The course in these cases is steadily downward despite operative intervention. The removal of the tumor is impossible, for it would necessitate removal of most of the brain stem at the involved level.

RUPTURED CEREBRAL VARICES

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When Pfannenstiel [1] described the first case of ruptured cerebral varix in 1887 he expressed the belief that the rupture was due to the intracranial congestion which occurred during eclamptic convulsions. In a second case studied by Kaufmann [2] the rupture occurred during eclampsia, lending support to the theory that toxemia of pregnancy in some way predisposes to the formation of cerebral varices.

Amsler [3] described two instances of cerebral varix, each occurring in the inconstant ophthalmomeningeal vein of Hyrtl. He expressed the belief that the anatomic position of this vein subjects it to possible trauma as it passes through the orbital fissure and that stasis in the vein itself or in the underlying sphenoparietal sinus might result in pressure of the vein against the sharp upper bony margin of the orbital fissure and in injury of the wall. Continued stasis might result in dilatation of the injured vein. However, in the report of a similar case by Anders [4] there were, in addition, other anomalous venous channels and numerous varicosities extending throughout the entire left cerebral hemisphere.

Beger [5] reported the occurrence of two varices in the tela choroidea of the third ventricle, one of which ruptured into the lateral ventricle. He concluded that congenital and probably hereditary weakness of the wall of the vein was responsible for its ultimate varicose condition. The

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1. Pfannenstiel: Apoplexie als tödlicher Ausgang von Eklampsie, Centralbl. f. Gynäk. **11**:601, 1887.

2. Kaufmann, E.: (*a*) Ueber Phlebektasie, Ztschr. f. Geburtsh. u. Gynäk. **37**:208, 1897; (*b*) Lehrbuch der speciellen pathologischen Anatomie, für Studierende und Aerzte, ed. 7-8, Berlin, G. Reimer, 1922, p. 122.

3. Amsler, C.: Ueber intrakranielle Varicenbildung an der Vena ophthalmomeningea Hyrtl, Frankfurt. Ztschr. f. Path. **11**:254, 1912.

4. Anders: Ueber ein Fall von ausgedehnter cerebraler Varicenbildung mit tödlicher Blutung in Verbindung mit Sinus pericranii, Beitr. z. allg. Path. u. path. Anat. **64**:540, 1918.

5. Beger, H.: Kasuistischer Beitrag zur cerebralen Varicenbildung, Virchows Arch. f. path. Anat. **231**:439, 1921.

description by Wohak [6] and by Marx [7] of large varices of the vein of Galen and the inferior longitudinal sinus, respectively, in new-born infants has strengthened the claim that varices may be of congenital origin or, at least, that their formation may be due to congenital defects in the structure of the veins.

Cerebral varix appears to be a clinical rarity. A careful review of the literature brought to light only twelve cases. Other types of cerebral venous anomalies are encountered not infrequently, especially by the neurosurgeon. These appear as anomalous or abnormally enlarged veins which result in neurologic symptoms [8] and may simulate tumor of the brain.[9]

REPORT OF CASES

CASE 1.—J. C., a white man, aged 41, a laborer, entered the Jewish Hospital on the night of Jan. 24, 1934, complaining of left hemiparesis, which began at 5 p. m. after an attack of vomiting while he was at work. Two weeks previously a similar attack of vomiting, lasting all day, was followed by no untoward symptoms. The general health had been good except that for six months prior to the present illness he had had frequent severe frontal headaches, vertigo, weakness and occasional bouts of vomiting.

Examination.—On admission the patient was quiet and drowsy, but he was easily aroused and answered questions intelligently and readily. There were no cardiac or respiratory symptoms. He had left hemiparesis, involving the face, arm and, to a less degree, the leg. The tongue deviated to the left. There was nuchal rigidity. The pupillary reflexes on the left were sluggish. The right pupil was smaller than the left. No weakness of any of the extrinsic ocular muscles was noted. There was inconstant bilateral nystagmus. The eyegrounds were normal. The reflexes on the right, both tendinous and cutaneous, were normal. On the left the biceps and triceps reflexes were exaggerated. The knee jerk on the left was equal to that on the right. Sustained ankle clonus and Babinski and Oppenheim signs were elicited on the left side. The abdominal and cremasteric reflexes were absent on the left. Neither the Hoffmann nor the Gordon sign was obtained. Kernig's sign was absent. Cutaneous sensibility to pinprick was normal, while no accurate responses to touch were obtained. The rest of the physical examination gave negative results. The blood pressure measured 120 systolic and 65 diastolic. The pulse rate was 75 per minute; the rectal temperature, 100 F. and the respiratory rate, 24 per minute.

Laboratory Findings.—The Kahn reaction of the blood was negative. The blood count was as follows: red cells, 5,680,000; white cells, 19,300; stab forms, 11 per cent; segmented forms, 77 per cent; lymphocytes, 10 per cent, and monocytes, 2 per cent. The urine was normal. The sugar content of the blood was 125 mg. per hundred cubic centimeters, and the nonprotein nitrogen content, 19 mg.

6. Wohak, H.: Ein Fall von Varix der Vena magna Galeni bei Neugebornen, Virchows Arch. f. path. Anat. **242**:58, 1923.

7. Marx, A. M.: Kongenitaler Varix des Sinus longitudinalis inferior, Med. Klin. **43**:1612, 1925.

8. Dandy, W. E.: Venous Abnormalities and Angiomas of the Brain, Arch. Surg. **17**:715 (Nov.) 1928.

9. Gordon, A.: Dilatation and Engorgement of Cortical Veins Simulating Tumor of the Brain, J. Nerv. & Ment. Dis. **70**:495, 1929.

Course.—There were deepening stupor and increase in the severity of the hemiplegia. On the day after admission to the hospital there was weakness of the right internal rectus muscle. A lumbar puncture at this time yielded bloody spinal fluid, containing about 2 per cent crenated red cells. The fluid was under markedly increased pressure. The Wassermann reaction of the spinal fluid was negative. The patient died with hyperpyrexia (a rectal temperature of 106 F. being present) and pulmonary edema. A diagnosis of subarachnoid hemorrhage due to rupture of an aneurysm at the base of the brain was made.

Necropsy.—Examination of the brain only was permitted at autopsy. Careful examination of the surface of the body failed to show evidence of varicosities of the skin. The scalp was normal. No venous anomalies were present in the calvarium. The dura was normal; the venous sinuses showed no abnormalities, either of structure or of location.

There was no subarachnoid hemorrhage, but the escaping cerebrospinal fluid was xanthochromic. The brain felt tense over the left parietal region, and to the palpating finger it gave the impression that intracerebral fluid under tension was present. The basal vessels (the circle of Willis and the basilar, vertebral and internal carotid arteries) were normal.

A frontal section of the brain, made through the level of the stalk of the pituitary gland, was followed by the escape of clotted and free blood from a cavity in the right cerebral hemisphere, involving the greater portion of the parietal and occipital lobes of that side and extending into the central portion and the occipital pole of the right lateral ventricle. The cavity measured approximately 10 cm. in its anteroposterior direction, extending to within about 5 cm. of the tip of the occipital lobe. The corpus striatum and the thalamus in their posterior portions were destroyed by the hemorrhage.

In an effort to locate the bleeding point, the clot and softened portions of the brain were washed away. It was observed that the arterial tree was of normal structure and was intact but that the venous tree appeared irregularly varicosed. After this observation, the venous tributaries of the great vein of Galen were dissected, beginning at the point where the great vein of Galen enters the straight sinus in the tentorium cerebelli. The left internal cerebral vein was normal in structure and relations. The right internal cerebral vein was dilated, tortuous and markedly enlarged. Of its tributaries, the choroid vein, the veins of the thalamus, the vein of the choroid plexus of the third ventricle and veins from the corpus callosum, the pineal body and the corpora quadrigemina were normal. The basal vein from the cerebral peduncle, the veins from the posterior horn of the lateral ventricle and the vena terminalis (draining the corpus striatum) were extensively varicosed. The veins appeared to be more numerous than in the normal condition. Those from the posterior horn of the lateral ventricle were massed together and thrombosed, and it appeared that one had ruptured, causing the bleeding. The hemorrhage extended from this point forward, involving the posterior portion of the cerebral peduncle, the corpus striatum and the internal capsule. The veins from the anterior portion of the corpus striatum were normal. The basal vein was thrombosed. Veins from the cerebellum were normal.

Sections were taken from several parts of the brain in the region of the plexus of varices. In addition, a section was taken from the right vein of Galen. Hematoxylin and eosin and Verhoeff's and Van Gieson's stain were used.

In the areas examined the normal architecture of the brain was destroyed by small extravasations of blood into the nervous tissue. Of particular interest was the presence of many closely packed, dilated, tortuous veins, varying greatly in size. Between these veins were innumerable capillaries, nerve fibers, glia cells

and minute hemorrhages. The extent of phagocytosis was minimal; some cells contained blood pigment; a few were laden with fat.

The veins were irregular in outline. The walls were of uneven thickness, varying in different parts of the same vein and in different veins. A few dilated veins of uniform thickness were present. For the most part the walls appeared hyalinized, and differential stains confirmed the comparative scarcity of muscle bundles and fibers in many veins or parts of veins.

The smaller veins were practically entirely composed of collagen fibers. No muscle or elastic tissue fibers were seen. The medium-sized veins usually showed muscle bundles in the media but consisted chiefly of connective tissue fibers. The intima was irregularly thickened. In some areas, especially where the wall was very thin, the line of demarcation between the intima and the internal layers of the media could not be identified. The internal elastic layer was absent at such places. In other portions of the vein the internal elastic layer appeared normal. At still other points this layer suddenly split into two or more lamellae, enclosing between them the excessive connective tissue fibrils that formed the intima. As a rule, the adventitia was entirely collagenous; no elastic fibrils could be seen (fig. *A*).

The large vein of Galen showed flat endothelium, hyalinized intima and loss of the internal elastic membrane, the faint outline of which could be identified in a few places. The media was thin and composed of intermingling of fibers of connective tissue and smooth muscle. No elastic tissue was present either in the media or in the adventitia. The adventitia consisted of dense collagenous tissue.

Cellular reaction was not uniform. Some smaller and medium-sized veins contained lymphocytes in the subendothelial and adventitial layers. A rare polymorphonuclear leukocyte could be identified. A moderate lymphocytic reaction was seen in the adventitia of the vein of Galen. Other veins examined in the same sections showed no cellular reaction.

In several larger veins thrombi of varying stages were present, the periphery of which showed varying degrees of organization.

CASE 2.—A white girl, aged 13, was brought to the St. Louis City Hospital on Oct. 6, 1934, in a semicomatose condition. She had been well until several hours prior to admission to the hospital, when she came home from play complaining of severe headache. She vomited shortly afterward and collapsed. The vomiting recurred and was of a projectile type. The past and the family history were unimportant, except that at the age of 7 years she had been admitted to the St. Louis Children's Hospital with fracture of the skull and other injuries, from which she recovered without apparent sequelae.

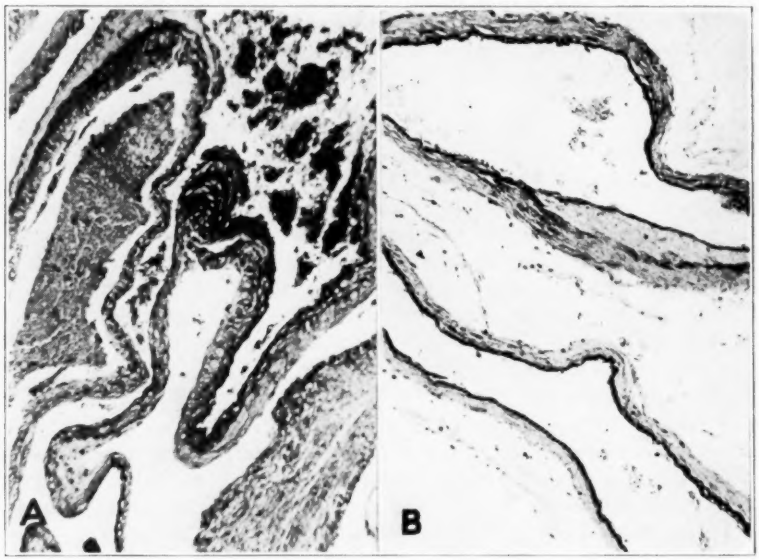
Examination.—The patient was well developed and well nourished. She appeared semiconscious, could be aroused and was restless and irritable. Only the following abnormal neurologic signs were noted: stiffness of the neck, an Oppenheim and a suggestion of a Babinski sign on the left and a questionable Kernig and a Brudzinski sign. The abdominal reflex on the right was sluggish; that on the left was normal. No motor weakness was present. The deep tendon reflexes were physiologic. The pulse rate was 64 per minute; the blood pressure was 130 systolic and 80 diastolic.

Course.—On Oct. 7, 1934, a small retinal hemorrhage and slight swelling of the margin of the disk were seen in the left eye; the right eyeground was normal. The spinal fluid was under a slight increase in pressure and was bloody and xanthochromic. The patient died suddenly on Oct. 9, 1934.

Necropsy.—A massive hemorrhage filled all the ventricles. The bleeding appeared to have come from the region of the left optic radiations and to have

ruptured into the posterior horn of the lateral ventricle. Within the substance of the disrupted tissue of the brain was a small mass, consisting of two small nodules and a plexus of veins which communicated with each mass. The plexus formed the communicating link between the two masses, which measured 10 and 7 mm., respectively, in their widest diameters. Each mass was, in reality, a small cyst filled with a blood clot, which was everywhere adherent to the inner surface of the wall of the cyst.

Each mass and the plexus of veins were sectioned serially and stained with the hematoxylin and eosin, Verhoeff and Van Gieson stains. Microscopic examination demonstrated the continuity of the vein of the plexus with the wall of each cyst. The wall of the cyst consisted entirely of collagenous connective tissue, which was so thinned in places that only a few connective tissue fibers supported the walls. No evidence of muscle or elastic tissue was observed in the wall.



A (case 1) is a section through a group of veins within the brain, showing the tortuous venous channels and the variation in the size and thickness of the vessels; *B* (case 2) is a section through a plexus of veins leading to a varix, showing the tortuosity of the vessels, the thickening of the intima and the splitting of the internal elastic membrane. Verhoeff's and the hematoxylin and eosin stain; × 75.

Elastic tissue was entirely lacking in the portion of the vein which joined the cyst, but at a distance from this junction the wall of the vein contained elastic fibers, which for the most part were fewer than normal and were arranged as lamellae. Only at a rather distant point from the cyst did the internal elastic membrane have a normal appearance. Muscle fibers were not seen in any veins in this section. The wall was composed of connective tissue. The intima was thickened and hyalinized and was rather prominently infiltrated with lymphocytes. There was a moderate amount of lymphocytic reaction in the adventitia. Large thrombi filled the cavities of the cyst. Peripheral organization was present. On the whole the microscopic appearance of the veins and varix in this case resembles that in the first (fig. *B*).

COMMENT

Since cases of varices of the brain are rare and there is only one report of this condition in the English literature, we have collected and summarized all the cases which we have been able to find.

SUMMARY OF CASES DESCRIBED IN THE LITERATURE

CASE 1 (Pfannenstiel [1] and Kaufmann [2b]).—A primipara, aged 22, was first observed when in coma. One week earlier she had vomited and suffered a brief convulsion, which did not recur until just prior to the loss of consciousness. Edema of the legs and backache were persistent symptoms in the last few days. On examination the patient appeared well developed. She was totally unresponsive to all stimuli. The pupils were widely dilated and fixed. The corneal reflexes were absent. The eyegrounds were unusually pale and the vessels were small; no other ophthalmoscopic changes were noted. No evidence of hemiplegia or defect of the cranial nerves was present. A catheterized specimen of urine became solid when boiled; microscopically, many casts but no blood cells were noted. Three hours after the induced delivery of a stillborn infant the patient died suddenly.

At autopsy, except a few minute subpial hemorrhages at the base and hyperemia of the meninges, the surface of the brain showed nothing extraordinary. A large hemorrhage, disrupting the substance of the brain in the region of the left optic thalamus, had ruptured into the left ventricle and filled all the ventricles with blood which had recently clotted. Hemorrhagic softening involved also the right optic thalamus, while a few petechial hemorrhages were scattered through the pons. The arteries were normal. A varix, about the size of a cherry seed, was located near the left optic thalamus. Microscopic examination proved the venous nature of the vessel, which had ruptured its thin wall. No varices were observed elsewhere in the body.

CASE 2 (Kaufmann [2b]).—A primipara, aged 23, died of eclampsia four hours after coming under observation. At autopsy, massive hemorrhage into the ventricles, the frontal lobes and the anterior portion of the corpus callosum was observed. Within the disrupted substance of the brain numerous small cysts, each containing adherent blood clots, were present. Their number is not stated. The walls of the cysts were composed of venous tissue, thinned in many places until only the serosa remained. One of the varicosed veins had ruptured, resulting in the death of the patient. No microscopic observations were reported.

CASE 3. (Amsler [3]).—A man, aged 46, had suffered from headache for some time. On June 13, 1910, he had a sudden convulsion, during which the mouth was drawn to the right. Convulsions recurred many times before death, two weeks later. Transient disturbances in the sensorium and speech occurred. Neurologic examination showed deviation of the uvula to the left, loss of deep tendon reflexes of the legs, a Babinski sign on the right, weak abdominal reflexes, early papilledema and venous congestive of the retina. A lumbar puncture on June 27 revealed a pressure of 17 cm. of water; the fluid was xanthochromic and contained numerous lymphocytes, and there was increase in the amount of gobulin. Six hours later the patient died suddenly.

At autopsy free subarachnoid hemorrhage was observed over the surface of the hemispheres, especially that of the right, and at the base of the brain. Free and clotted blood was present in all the ventricles. The right gyrus hippocampus and the inferior portion of the right optic thalamus contained hemor-

rhages. At the right orbital fissure, lying against the skull, was a mass about 1 cm. in diameter, which contained blood. This proved to be a ruptured varicosity of a communicating vein between the middle cerebral and the superior orbital vein. This anomalous vein in its course passed through the orbital fissure. The dura at this point was uninvolved. Bleeding into the right eyeground was present.

Microscopic examination of the wall of the undilated portion of the vein showed that the intima consisted of a smooth layer of endothelial cells, connective tissue and a fine elastic membrane. The media was lacking. The adventitia was strong and was composed of crossed bands of connective tissue, a few elastic fibers and peripheral bundles of smooth muscle fibers. At the site of the varicosity the wall of the vein was considerably thinned, and the adventitia was infiltrated by many lymphocytes and a few leukocytes. The elastic tissue of both the intima and the adventitia was reduced, while the muscle bundles appeared to be hyalinized. A partially organized thrombus was attached to the wall opposite the site of the perforation. The dura in the region of the varix was somewhat infiltrated by lymphocytes.

Case 4 (Amsler [3]).—A woman, aged 50, with carcinoma of the breast metastasizing to the spine and right femur, was admitted on Oct. 15, 1911, with vomiting and disorientation. On November 15 speech became defective. The patient was excited and cried out often. On Nov. 18, 1911, she died.

Autopsy showed sclerosis of the basal arteries. In the left first temporal gyrus of Wernicke were several small hemorrhages. The temporal vein draining this region was thrombosed. At the orbital fissure, lying against the edge of the orbital portion of the sphenoid bone, was a dilated vein, measuring 5 by 5 by 4 mm. This vein passed through the lateral half of the orbital fissure to form a communication between the left superior orbital and the left middle cerebral vein. At one point in its course this vein lies with the sphenoparietal sinus below and the sharp edge of the sphenoid bone above. There was no rupture of the varix, nor had bleeding occurred. The dilated vein contained a thrombus, adherent to the wall. The wall of the vein was markedly thinned in places, but thickening also occurred. Microscopic examination of the dilated vein showed the following structure: The intima, wherever it was free from the formation of thrombi, was lined with a layer of flat endothelial cells. A thin layer of connective tissue disrupted the internal elastic membrane. The media was absent. The greater portion of the wall of the vein was composed of adventitia, which consisted of layers of hyalinized connective tissue bundles, poor in cells. Interspersed between these bundles were a few isolated elastic tissue fibers. At the periphery smooth muscle fibers were present.

The greater the dilatation of the vessels the fewer were the elastic tissue fibers which entered into the structure of the wall. Wherever the wall of the vessel was thickened, in part or as a whole, the increase in the size of the wall was due to excessive formation of connective tissue.

Thrombi were partially organized. No evidence of inflammation existed in this case.

Case 5. (Anders [4]).—A man, aged 25, a stretcher bearer during the war, after a heavy night's work suddenly showed signs of distress, became aphasic and had convulsions, which recurred during the day. During the lucid periods well marked aphasia persisted. He died suddenly the next day.

Autopsy showed abnormalities in the head only. The rest of the body was free from venous anomalies. Over the left portion of the frontal bone, beneath the scalp, were three venous cysts which communicated with the diploic veins of the skull. The outer table of the skull was excavated by these cysts.

In the left hemisphere of the brain multiple hemorrhages were present, extending from the frontal to the occipital lobe, involving most extensively the basal ganglia and the external and, to a slight degree, the internal capsule. Numerous dilated veins, tributaries of the vena terminalis sinistra, contained thrombi and possibly had ruptured. No bleeding had invaded the ventricles.

The left middle cerebral vein was markedly dilated and contained numerous varicosities. Its diameter at the point where it penetrated the substance of the brain was from 3 to 4 mm. It contained partially organized thrombi; possibly this vein had ruptured within the substance of the brain. An anomalous branch of the middle cerebral vein, the so-called ophthalmomeningeal vein of Hyrtl, extended forward, passing through the superior orbital fissure to join the superior orbital vein. It was markedly dilated and varicosed and was completely thrombosed throughout its course.

Microscopic examination of the wall of the vein showed only an organizing thrombus. No evidence of syphilis was present.

CASE 6 (Beger [5]).—A housemaid, aged *22*, was suddenly seized with symptoms of intracranial disturbance on the day before she was admitted to the hospital. Twelve years earlier she had meningitis, and since then periodic headaches had occurred. When first examined the patient was in deep coma. Nuchal rigidity, meningismus and spastic paresis of the lower extremities were present. The reflexes were exaggerated; the Babinski sign was present bilaterally. There was no fever. The spinal fluid was under increased tension and consisted almost entirely of blood.

On the following day vomiting and convulsions occurred. Ophthalmoscopic examination revealed papilledema on the left side. Convulsions increased in frequency of occurrence and severity; the temperature became elevated, and the patient died five days after the onset of symptoms.

At autopsy the dura over both frontal lobes was observed to be under tension. Small subarachnoid hemorrhages were present over the cortex and at the base of the brain. The corpus callosum bulged between the two hemispheres, and when it was cut large amounts of fluid blood were liberated from each ventricle. Blood clots were also present. Hemorrhage had extended into all the ventricles.

In the tela choroidea of the third ventricle, two globular nodules on the right internal cerebral vein protruded into the right lateral ventricle. One was the size of a pea; the other, one-half that size. A slitlike rupture was present in the smaller of these varices. The choroidal arteries were normal.

No varices were noted elsewhere in the body.

Microscopic examination of the veins showed replacement of the muscle fibers by fibrous and hyaline tissue. Thrombi showed early organization. No evidence of inflammatory reaction was observed.

CASE 7 (Wohak [6]).—A boy came to autopsy twenty-four hours after birth. He had died with symptoms of a lesion in the posterior fossa. The mother was a primipara, aged 24, who had been in labor for twenty-four hours. Delivery was spontaneous. Sudden asphyxia was temporarily improved by artificial respiration. No congenital anomalies were noted.

At autopsy bilateral rupture of the tentorium cerebelli was noted on each side of the insertion of the falx. Within the confines of the tear was a hematoma the size of a small apple, which protruded upward between the two cerebral hemispheres and behind the corpus callosum, encroaching on both occipital lobes. This mass was covered by a thin-layered membrane, which communicated anteriorly with the veins of Galen and posteriorly with the inferior longitudinal sinus and

occupied the place in which the great vein of Galen is normally situated. The wall of the cyst was not ruptured. Its contents consisted of coagulated blood.

Microscopically, the intima was seen to consist of a layer of flat endothelial cells. The media contained smooth muscle fibers, but the thickness and strength varied in different places. The adventitia, consisting of connective tissue, also varied in thickness. The internal cerebral veins were of normal histologic structure.

Case 8 (Marx [7]).—A child, aged 3 days, came to autopsy after sudden death. The mother, aged 19, a primipara, was delivered spontaneously and rapidly. The infant was of normal size and development.

At autopsy the straight sinus was seen to be dilated to form a sac 3 cm. long by 1.7 cm. high by 1.2 cm. wide lying in the normal course of the sinus and emptying into the sinus confluens. The wall was of variable thickness, approaching that of paper at some points. The varicosed sinus was filled with coagulated blood, and it had made an impression on the overlying occipital lobes.

Microscopically, the wall varied considerably in thickness; at the point of attachment of the falx it was very thick, while laterally it was thinned to a marked degree. In such places the media was deficiently developed, and in several instances it was absent. There also the adventitia was diminished, so that the wall consisted of intima and a thin layer of connective tissue. Elastic fibers were inconstant in their distribution, being least numerous where the wall was thinnest.

Case 9 (Pol [10]).—An infantryman, aged 38, suddenly had crossed paralysis: right hemiplegia with paresis of the left side of the face. A diagnosis of pontile hemorrhage or tumor was made. Seven years later the patient died suddenly.

At autopsy it was observed that a varix, measuring 7 by 7 by 7 mm., lying to the left of the midline of the pons, had ruptured. It was a tributary of the inferior cerebral vein. Owing to its size it had produced an impression on the pons, which explained the preexisting paralysis. No report of a microscopic examination is available.

Case 10 (case records of the Massachusetts General Hospital [11])—A boy, aged 12 years, died of acute appendicitis and peritonitis. Sixteen months earlier he had suffered left hemiplegia, from which he had partially recovered. At the time the spinal fluid was bloody and xanthochromic. A diagnosis of subarachnoid hemorrhage had been made.

Autopsy revealed in the right anterior central convolution a collection of thin-walled veins forming a mass, 0.5 cm. in diameter, extending into the substance of the brain for a distance of 2 cm. The vessels ranged from 3 or 4 mm. to less than 1 mm. in diameter. On the surface the veins were dilated in the upper part of the rolandic region of the right hemisphere. No hemorrhage was present at that point. On the mesial aspect of the anterior central convolution, an area of old softening, stained with hemosiderin, extended from the cortex of the upper portion of the rolandic region to the corpus callosum.

Microscopically, the veins had irregularly thickened walls, owing to an increase of connective tissue. The adjacent portion of the brain was scarred by loose connective tissue.

Reference was made to two other cases,[10] but no description had been found in the literature.

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10. Pol: Varix auf der Ponsbasis mit Ruptur, München. med. Wchnschr. **74:** 1208, 1927.

11. Case Records of the Massachusetts General Hospital, Case 18381, New England J. Med. **207:**547, 1932.

COMMENT

An analysis of twelve cases of cerebral varix, including the two reported in this paper, showed that they are equally divided between the sexes, six occurring in males and five in females. The sex was not reported in one case. The disease is more common in young persons, eight patients being 25 years or under: two new-born infants, two children and four adults between the ages of 22 and 25. The ages of the remaining four patients ranged from 38 to 50.

Clinically, the presence of cerebral varix was unsuspected in all the cases reported. In one instance the varix gave no clinical symptoms; it was accidentally discovered at autopsy. In the two cases of new-born infants, death was produced by increased intracranial pressure caused by a rapidly expanding varix. Rupture of the varix with fatal hemorrhage occurred eight times; without fatal hemorrhage, once. Sudden increases in intracerebral pressure preceded fatal rupture four times: twice during eclamptic convulsions and twice during severe physical exertion. In one case in which the initial symptom followed trauma of the head sustained during the war, symptoms of pressure persisted for seven years before death from rupture occurred.

The sites of these vascular lesions were of particular interest. Three occurred in the anomalous ophthalmomeningeal vein of Hyrtl, while in a fourth case there was congenital malformation of the varicosed vein of Galen. In a total of seven cases there was involvement of the vein of Galen or of its tributaries or terminus. The pontile vein was varicosed in one case. There was only one instance of involvement of cortical veins.

Cellular infiltration of the wall of the vein was present in three cases. Amsler reported lymphocytic reactions in one case, while in both the present cases a similar invasion of the wall of the vein was observed. We do not believe that the cellular reaction is evidence of a primary inflammatory process or that inflammation is productive of varices. Certainly, in our studies the most striking picture was that of sclerosis of the vein: Connective tissue replaced in varying degrees the muscle and elastic tissue elements of the venous wall; the internal elastic membrane, when it was not completely destroyed, was split into lamellae, and the intima in its thickening and hyalinization resembled closely that of an arteriosclerotic vessel. Probably the cellular reaction was a result rather than the cause of the degenerative process. In eleven of the cases in which analysis was made no evidences of inflammation were observed.

The pathologic processes described in cases of varicosity lack uniformity, but this is probably due to failure on the part of investigators to consider that the degree of involvement may vary not only in different parts of the same vein but in portions of a cross-section. All the authors

agree that there is no change in the endothelium unless the vessel is thrombosed. At this point agreement ends. Nicholson [12] reviewed the conflicting opinions and discussed in detail the observations of Zancani,[13] with whom his own agreed closely. Briefly, these authors noted that there is an increase in connective tissue and a decrease in muscle and that replacement of the essential tissue elements by supporting tissue occurs. Varying degrees of atrophy of the muscle, degeneration and fragmentation of elastic fibers and increase in connective tissue are the principal changes. In places the degeneration has advanced to such a degree that the muscle has disappeared entirely, and the wall has the appearance of homogeneous, dense connective tissue.

These observations correspond exactly with those made in the present cases, and they agree well with the descriptions which are available in six of the other cases reported. In each instance the defect in the media, the deficiency of elastic tissue and the striking increase in collagenous connective tissue are stressed. It is significant that in the two cases of varices in the new-born, in which the lesion was unquestionably congenital, the media is described as being deficient in muscle tissue. In one of these cases the elastic tissue is described as inconstant and as most deficient in the thinnest part of the wall. Certainly, the appearance of the walls of the veins is characteristic of a degenerative process which might occur in a case of phlebosclerosis. Presumably, any congenital malformations which may exist may be modified by this sclerosis, so that the characteristic hyalinization may be present in the older patients, while in the younger persons deficiencies in the wall of the vein without fibrosis and hyalinization may be the presenting picture.

The etiology of varicosed veins in general has not been definitely established. Lehmann [14] reviewed the prevailing conceptions of the causes of varicosity. Mechanical factors, inflammation, degenerative processes, phlebosclerosis as a system disease and congenital defects, primarily in the formation of veins or as part of a generalized defect in the mesenchyme, were important causes suggested in the discussion. Probably, a combination of these underlying factors plays a part in individual circumstances. We believe that congenital defects in the wall of the vein are probably the most important etiologic factor in the production of a cerebral varix. The age incidence supports this point of view. The defects in the structure of the venous wall in the newborn infants also strengthen this conception. The occurrence in one third of these cases of other venous anomalies in the brain suggests that

12. Nicholson, B. B.: Histopathology and Etiology of Varicose Veins, Arch. Surg. **7**:47 (July) 1923.

13. Zancani, A., cited by Nicholson.[12]

14. Lehmann, E.: Ueber Aetiologie, Pathogenese und histologische Struktur von Varizen, Frankfurt. Ztschr. f. Path. **32**:300, 1925

anomalous structures of the walls may be coexistent. We are particularly impressed by the localization of the lesion in the vein of Galen and its tributaries in a large majority of the cases. This may be the result of an inherent developmental defect in the wall of this vein, to which is added the stress which exists at the entrance of the vein into the firmly fixed straight sinus. The sinus is suspended in the inferior margin of the falx cerebri at its insertion into the tentorium cerebelli, which is in a more or less fixed position in relation to the cranium, while the vein of Galen lies in relation to a part of the brain which is somewhat movable, particularly at this point. We can suggest only that this mechanical factor and probably others which are not altogether clear at this time may enter into play because of this anatomic relationship. Amsler and Anders expressed the belief that obstruction of the venous outflow of the ophthalmomeningeal vein at the orbital fissure produced stasis which resulted in the formation of a varix. This vein, like the vein of Galen, passes at its mouth from a relatively movable to a fixed point. It is necessary to regard this fact as an important influence in the production of varices of the vein of Hyrtl.

In the cases of Wohak and Marx the stasis in the cerebral veins occurring during birth seemed to have affected the already weakened walls. The effect of trauma in the production of rupture of these varices appears to be clear, as we have already mentioned. The part which mechanical factors may have played in the production of varices in the other cases is not clear.

CONCLUSIONS

Two cases of cerebral varix are described, and ten cases collected from the literature are reviewed.

The vein of Galen or its tributaries and the anomalous vein of Hyrtl are the common sites.

Phlebosclerosis is a common histologic picture in cases of older persons.

The most important apparent etiologic factor is the congenital defect of the wall of the vein.

MULTIPLE SCLEROSIS

EFFECT OF TYPHOID VACCINE AND OF EPINEPHRINE ON COAGULATION OF THE BLOOD

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AND
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BOSTON

Seventy years ago Leyden,[1] in one of the earliest papers on multiple sclerosis, pointed out that exposure to cold and dampness, concussions to the body and and psychic trauma appear to play a significant rôle in the onset and perhaps in the etiology of the disease. These factors have been pointed out by others.[2] In 1922 the commission on multiple sclerosis of the Association for Research in Nervous and Mental Diseases concluded that in a certain percentage of cases the onset of the disease is associated with trauma or infection.[3] Exacerbation of the symptoms after trauma, operation, exposure, immersion, pregnancy, infection or severe emotional excitement have long been recognized.

A common mechanism in these apparently unrelated conditions was suggested by Putnam's recent work[4] on the pathology of multiple

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1. Leyden, quoted by Timme, Walter, in Dana,[3] p. 5.

2. Berger, A.: Eine Statistik über 206 Fälle von multipler Sklerose, Jahrb. f. Psychiat. u. Neurol. **25**:168, 1905. Jelliffe, S. E.: Multiple Sclerosis: Its Occurrence and Etiology, J. Nerv. & Ment. Dis. **31**:446, 1904. Marie, P.: Sclérose en plaques et maladies infectieuses, Progrès méd., 1884, pp. 287, 305, 349 and 365. Oppenheim, H.: Aerztliches Gutachten betreffend die Erkältungs-Aetiologie der multiplen Sklerose, Med. Klin. **7**:1517, 1911. Palmer, W. T.: Case of Disseminated Sclerosis Following Injury, West London M. J. **12**:219, 1907. Woodbury, M. S.: A Probable Etiologic Factor in Multiple Sclerosis, Arch. Neurol. & Psychiat. **1**:408 (April) 1919.

3. Dana, C. L.: Multiple Sclerosis, New York, Paul B. Hoeber, Inc., 1921, vol. 2.

4. Putnam, T. J.; McKenna, J. B., and Morrison, L. R.: Studies in Multiple Sclerosis: I. The Histogenesis of Experimental Sclerotic Plaques and Their Relation to Multiple Sclerosis, J. A. M. A. **97**:1591 (Nov. 28) 1931. Putnam, T. J.; McKenna, J. B., and Evans, J.: Experimental Multiple Sclerosis in Dogs

sclerosis. Putnam advanced experimental evidence indicating that the pathologic changes in the disease are the result of multiple small venous thromboses in the brain and spinal cord, with resulting ischemia and stimulation of the macroglia to proliferation and formation of areas of gliosis. Cannon [5] demonstrated that blood coagulates more rapidly after the injection of epinephrine or after emotional excitement. Hartman [6] and Mills, Necheles and Chu [7] noted the same effect. Von Falkenhausen [8] noted an increased tendency to intravascular thrombosis after the injection of Bacillus prodigiosus. König [9] and others [10] showed that there is increased coagulability of the blood after operation or after fever. These considerations led to the investigation of the blood of patients with multiple sclerosis.

In a preliminary study routine examinations of the blood were made on a small group of patients with multiple sclerosis. The red cell count, the white cell count, the hemoglobin content, observations on the blood smear, the bleeding time, the clotting time, the platelet count and the sedimentation rate were within normal limits. A functional test was then sought to determine whether the blood of patients with multiple sclerosis reacts differently to certain agents from the blood of normal persons. The intravenous injection of typhoid vaccine was chosen as an experimental means of simulating acute infection, and epinephrine was administered subcutaneously to reproduce the physiologic effects of emotional excitement.

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from Injection of Tetanus Toxin, J. f. Psychol. u. Neurol. **44**:460, 1932. Putnam, T. J.: Pathogenesis of Multiple Sclerosis, New England, J. Med. **209**:786, 1933; The Biological Significance of the Lesions of Multiple Sclerosis, Science **80**:295, 1934; Studies in Multiple Sclerosis: IV. "Encephalitis" and Sclerotic Plaques Produced by Venular Obstruction, Arch. Neurol. & Psychiat. **33**:929 (May) 1935.

5. Cannon, W. B.: Bodily Changes in Pain, Hunger, Fear and Rage, New York, D. Appleton & Company, 1929, chaps. 9 and 10.

6. Hartman, F. A.: Changes in the Clotting Time of the Blood of Cats as a Result of Exercise, Am. J. Physiol. **80**:716, 1927.

7. Mills, C. A.; Necheles, H., and Chu, M. K.: Relation of Clumping and Disintegration of Platelets to Body Metabolism, Chinese J. Physiol. **2**:219, 1928.

8. von Falkenhausen, M.: Untersuchungen über den Regulations-mechanismus von Störungen der intravasalen Ungerinnbarkeit des Blutes bei experimentellen Beeinflussing der Gerinnungsfaktoren durch Bakterien, unspezifische Reizkörper und Witte-Pepton, Arch. f. exper. Path. u. Pharmakol. **142**:342, 1929.

9. König, W.: Experimentelle Untersuchungen über die Entstehung der Thrombose, Arch. f. klin. Chir. **171**:447, 1932.

10. Hirsch, H.: Die Beeinflussung der Serumeiweisskonzentration und Fraktion des menschlichen Serums durch Diathermie, Arch. f. exper. Path. u. Pharmakol. **156**:346, 1930. Heusser, H.: Postoperative Blutveränderungen und ihre Bedeutung für die Entstehung der Thrombose, Deutsche Ztschr. f. Chir. **210**:132, 1928.

PROCEDURE

In twelve patients with multiple sclerosis and in fourteen control patients the clotting time of the blood was studied with reference to the changes produced by the intravenous injection of typhoid vaccine and by the subcutaneous injection of epinephrine. Care was taken to select patients with multiple sclerosis in whose cases the diagnosis was beyond reasonable doubt. In all cases the disease had existed for several years, with characteristic remissions and exacerbations. Each patient had had one or more periods of observation in the hospital, with complete laboratory study, including examination of the cerebrospinal fluid. The control patients were chosen as far as possible in the same age group. The average age of the patients with multiple sclerosis was 32, the youngest being 18 and the oldest 43. The average age of those in the control group was 29, the youngest being 16 and the oldest 45. The control group comprised five patients with psychoneurosis, five with epilepsy and one each with postencephalitic parkinsonism, tumor of the brain, neuromuscular dystrophy and syringomyelia.

The clotting time was estimated by a modification of the Howell method. By means of a tourniquet, blood was drawn from a vein of the arm into an oiled syringe. Care was taken to have the needle enter the vein directly so as to avoid the addition of tissue juices or air bubbles, either of which would lower the clotting time materially. A small amount of blood (from 0.5 to 1 cc.) was allowed to flow down the sides of each of a series of fifteen small oiled test tubes. Every precaution was taken not to disturb the blood more than was necessary in transferring it from the vein to the tubes or thereafter. The test tubes, needle and syringe had been previously prepared by rinsing with a solution of three parts ether to one part liquid petrolatum. The tubes had been inverted and allowed to drain for approximately thirty minutes, in which time the ether evaporated, leaving a thin coating of oil on the glass. After the blood had been placed in the tubes one tube was inverted every five minutes until clotting occurred. After a tube was inverted and it was found that the blood had not coagulated, the tube was discarded, since the disturbance thus produced is enough to make the blood clot more rapidly thereafter. When a tube was inverted and the blood was found to be clotted, the next two tubes were also inverted. If these likewise showed clotting, this time was called the end-point. If either of the next two tubes did not show clotting, a plus-minus (±) was assigned to that time, and another tube was inverted five minutes later until the end-point was reached. The end-point was taken as the clotting time except when two or more plus-minus readings appeared in a series of determinations, when an average was taken for the clotting time. Normal subjects by this method showed a clotting time ranging from twenty-five to forty-five minutes. The method is accurate to within five minutes. A change of less than ten minutes was not considered significant.

By the method described for determining the clotting time, two sets of experiments were conducted on each patient.

Determination of the Clotting Time After the Intravenous Injection of Typhoid Vaccine.—In these experiments the first determination of clotting time was made at about 8 a. m., and the patient was then given an intravenous injection of 200 million typhoid bacilli. Further estimations of clotting time were made two, five, eight, twenty-four, thirty-two, forty-eight and seventy-two hours later. On the first day the patient was not given food until after the eight hour determination. On the second, third and fourth days breakfast was withheld until after the clotting time was estimated. The thirty-two hour determination was made before the

patient was given supper. A chart showing the temperature taken every hour was kept during the course of the fever.

Determination of the Clotting Time After the Subcutaneous Injection of Epinephrine.—The patient fasted throughout the period of the experiment. After the clotting time was first estimated, 1 cc. of a 1: 1,000 solution of epinephrine was injected subcutaneously, and the clotting time was estimated one, two, three and four hours later. Medication was not permitted during any of the experiments. The patient was permitted to drink water, but not to smoke. Excitement and emotion of any kind were guarded against as far as possible.

In one additional control patient, in whose case the diagnosis was psychoneurosis, blood was drawn under the same circumstances and at the same times as in the experiments with typhoid vaccine, but an injection of typhoid vaccine was not given, in order to determine how constant the clotting time remains under these conditions.

RESULTS

The Effect of the Intravenous Injection of Typhoid Vaccine on the Clotting Time.—A marked drop in the clotting time was associated with a chill and the rise in temperature. The degree of the drop was not significantly different in the two groups of patients, averaging twenty-three minutes, or 54 per cent, for the group with multiple sclerosis and seventeen minutes, or 47 per cent, for the controls. The duration of the fever was not materially different in the two groups, averaging thirty hours for the group with multiple sclerosis and twenty-seven hours for the controls. The degree of fever was not materially different. However, there was a striking difference in the duration of the drop in clotting time. The average duration of the drop was sixty-nine hours for the group with multiple sclerosis as contrasted with twenty-six hours for the control group. By using the unit "per cent hours" (1 per cent hour meaning a drop of 1 per cent of the original clotting time lasting for one hour), one can obtain a measure of the total drop, embracing the degree and the duration. For the group with multiple sclerosis there was an average drop of 1,971 ($\pm$ 272) per cent hours as contrasted with an average drop of 760 ($\pm$ 102) per cent hours for the controls (chart 1).

Of the twelve patients with multiple sclerosis eight gave a reaction to the typhoid vaccine in a manner similar to the average for the patients with multiple sclerosis shown in chart 1. Two gave a reaction similar to the average for the controls, and 2 gave a reaction which could not be placed definitely in either of the aforementioned groups. Of the fourteen control patients, only one gave a reaction similar to the average for the patients with multiple sclerosis.

In one control patient who did not receive typhoid vaccine there was no significant change in the clotting time throughout the course of the experiment.

The Effect of the Subcutaneous Injection of Epinephrine on the Clotting Time.—There was an even more marked difference in the two groups in this experiment than in that with typhoid vaccine, in regard to both degree and duration of the drop in clotting time. The average maximum drop for the group with multiple sclerosis was nineteen minutes, or 45 per cent, as contrasted with four minutes, or 11 per cent, for the control group. The average duration of the drop was three and seven-tenths hours for the group with multiple sclerosis, and one hour for the control group. The total drop for the group with multiple sclerosis was 87 ($\pm$ 8) per cent hours and for the control group, 16 ($\pm$ 5) per cent hours (chart 2).

Each of the twelve patients with multiple sclerosis showed a definite drop in clotting time following the injection of epinephrine. Of the fourteen control patients, nine showed no drop in the clotting time, four gave a reaction similar to that of the patient with multiple sclerosis, and the reaction of one was indefinite.

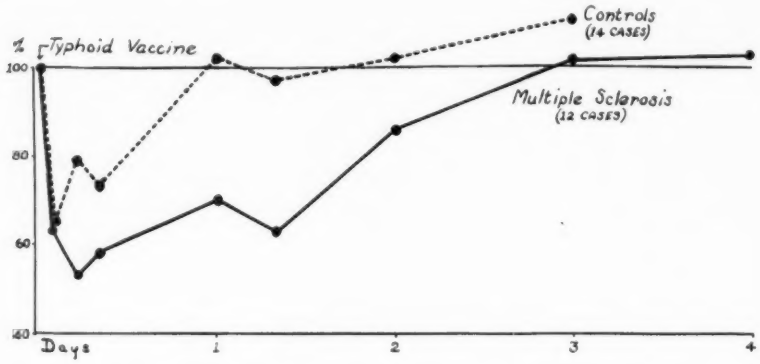

Chart 1.—The effect of the intravenous injection of typhoid vaccine on the clotting time of the blood. The ordinates represent the percentage of the original clotting time before the vaccine was given, and the abscissas, the time in days. The solid line is the curve of the average clotting time for twelve patients with multiple sclerosis, and the dotted line, the curve of the average clotting time for fourteen patients used as controls.

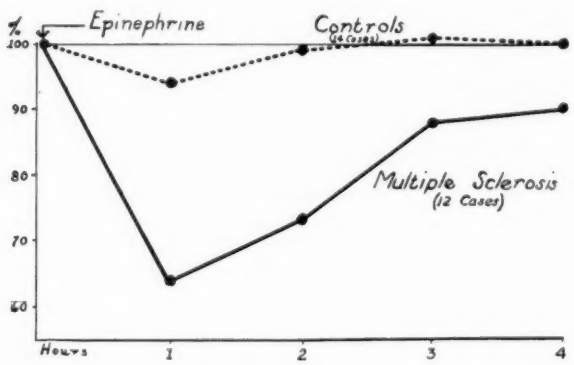

Chart 2.—The effect of the subcutaneous injection of epinephrine on the clotting time of the blood. The ordinates represent the percentages of the original clotting time before the epinephrine was given and the abscissas, the time in hours. The solid line is the curve of the average clotting time for twelve patients with multiple sclerosis, and the dotted line, the curve of the average clotting time for fourteen patients used as controls.

COMMENT

While this series of cases is small, the results suggest that there may be an abnormality in the coagulation of the blood in some patients with multiple sclerosis. This abnormality apparently consists in an increased lability of the clotting time, as a result of which such influences as typhoid vaccine and epinephrine produce more marked and more prolonged changes than in control patients. Such an abnormality would make clearly for an increased tendency toward intravascular clotting and would lend support to Putnam's observations on the pathology of the disease. It is noteworthy that the various factors associated with the onset or exacerbation of the symptoms of multiple sclerosis are known to be associated also with either an increased rapidity of coagulation of the blood or an increased secretion of epinephrine, which in turn causes increased rapidity of coagulation.

Further work is now in progress involving the study of the blood platelets and chemical analysis of the blood, with special reference to the elements entering into coagulation.

SUMMARY

The reaction of the clotting time of the blood to the intravenous injection of typhoid vaccine and to the subcutaneous injection of epinephrine was determined in twelve patients with multiple sclerosis and in fourteen controls.

In the experiments with typhoid vaccine the degree of the drop in clotting time was not significantly different in the two groups of patients, averaging twenty-three minutes, or 54 per cent, for the group with multiple sclerosis and seventeen minutes, or 47 per cent, for the controls. The duration of the fever was thirty hours in the group with multiple sclerosis and twenty-seven hours in the controls. There was a striking difference in the duration of the drop in clotting time, the average duration of the drop being sixty-nine hours for the group with multiple sclerosis, as contrasted with twenty-six hours for the control group. There was considerable individual variation in each group.

In the experiments with epinephrine there was a marked difference between the groups, in regard to both degree and duration of the drop in clotting time. The average maximum drop for the group with multiple sclerosis was nineteen minutes, or 45 per cent, as contrasted with four minutes, or 11 per cent, for the controls. The average duration of the drop was three and seven-tenths hours for the group with multiple sclerosis and one hour for the control group. There was considerable individual variation in each group.

The possible etiologic significance of these findings is discussed.

Clinical Notes

AN INK-WRITING ELECTRO-ENCEPHALOGRAPH

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The electrical potentials generated in the cerebral cortex may ultimately have considerable clinical as well as physiologic significance. Preliminary observations on these phenomena were carried out with a string galvanometer and a direct current amplifier [1] and with a cathode ray oscillograph and a capacity-coupled amplifier,[2] but it was soon evident that the most significant electrical waves had frequencies below 30 cycles per second and might therefore be successfully recorded by means of an ink-writing oscillograph. The advantages of obtaining an immediate permanent record on a paper tape at a cost of 1 cent per hundred feet are obvious. The problem was to obtain an ink-writing oscillograph with as high a frequency range as possible and to construct an amplifier to deliver to it sufficient current for its operation. Ink-writing oscillographs for this purpose have already been developed by Toennies [3] and by Adrian and Matthews,[4] but we believe that the principle of our output amplifier represents a useful addition to oscillographic technic.

Through the courtesy of Mr. J. W. Milnor of the Western Union Telegraph Company, several Boehme type 2-A undulators were obtained and converted to our uses. The "undulator" comprises a moving magnetic element which operates a small silver siphon writing on a moving strip of paper. As in the case of all mechanical oscillographs, the amplitude of the response is a function of the frequency of the oscillations, but it was found possible, by increasing the restoring force of the undulator springs and adjusting the pressure of the siphon on the tape to provide just-critical damping, to obtain good records at all frequencies up to 40 cycles per second. The relative suppression of higher frequencies has real practical advantages in that it greatly reduces any 60 cycle artefact, which often appears if the subject is not in a shielded room, and minimizes the disturbances due to muscular action potentials from the neck or jaw. The width of the paper tape was increased from ⅜ to ⅝ inch (0.96 to 1.6 cm.) so that larger amplitudes than usual could be used. This also provided an ample margin for a second pen to record time intervals of one second and also signals indicating stimulation, activity of the subject and the like. The speed of the tape can be

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This investigation was aided by a grant from the Josiah Macy Jr. Foundation.

1. Garceau, E. L., and Forbes, A.: A Direct-Coupled Amplifier for Action Currents, Rev. Scient. Instruments **5**:10, 1934.

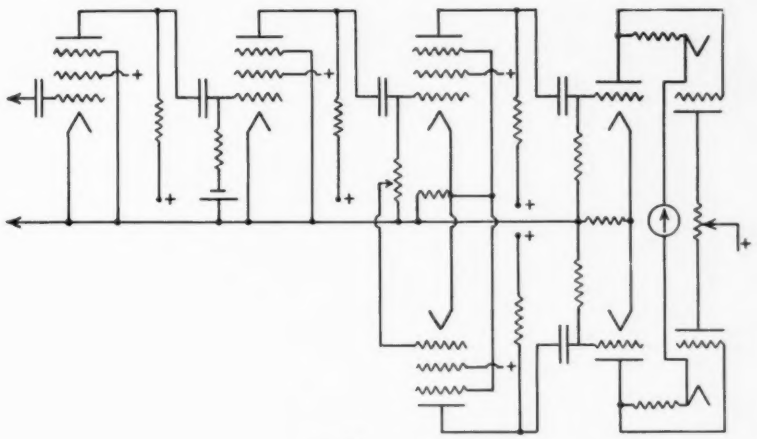
2. Garceau, E. L., and Davis, H.: An Amplifier, Recording System, and Stimulating Devices for the Study of Cerebral Action Currents, Am. J. Physiol. **107**:305, 1934.

3. Toennies, J. F.: Der Neurograph, ein Apparat zur Aufzeichnung biolektrischer Vorgänge unter Ausschaltung der photographischen Kurvendarstellung, Naturw. **20**:22, 1932.

4. Adrian, E. D., and Matthews, B. H. C.: The Berger Rhythm: Potential Changes from the Occipital Lobes in Man, Brain **57**:355, 1934.

adjusted by a positive friction gear from ½ inch to 5 inches (1.27 to 12.7 cm.) per second.

This instrument requires an unusually large amount of power for its operation, particularly if it is desired to write a large record on the wide tape. A portable amplifier consisting of two units was developed to provide the necessary amplification. The first unit is operated by a battery and consists of three stages of resistance-capacity-coupled high-μ pentodes with the last of the three stages in push-pull. The obvious objection to this circuit is that when the condensers and grid leaks are made large enough to pass low frequencies, some annoyance is caused by the blocking of the amplifier when large contact potentials are applied to the input. In order to conserve weight and obtain reliability of operation, however, it has seemed advisable to continue using condensers as large as 4 microfarads with 1 megohm leaks. This allows the use of common B batteries and A batteries. When the electrodes are properly applied, particularly with the subcutaneous needle electrodes, there is little trouble from blocking in the course of an experiment.



Amplifier circuit.

The output unit is operated on the 110 volt, 60 cycle mains. The amplifier is a four tube modification of the Wold and Wynn-Williams vacuum tube bridges.[5] In this circuit, as will be seen from the accompanying diagram, the grids of two tubes in push-pull are excited 180 degrees out of phase by the output of the push-pull (third) amplifier stage. The other two arms of the bridge are also vacuum tubes of the same type (2A3). They are so connected that when the bridge is thrown out of balance by a signal appearing on the input grids and in consequence a cross current appears in the load (in this case the undulator magnet) this current passes through the cathode drop resistors of the second pair of tubes and unbalances these arms of the bridge. This bridge connection is a comparatively efficient way of inserting a load into the plate circuit of an amplifier and of balancing out the direct current component of the plate current. An exceptionally long linear characteristic can be obtained without excessive plate

5. Wold, P. I.: Thermionic Amplifying Circuit, U. S. Patent 1,232,879, July 10, 1917.

voltages. The small potentiometer between the plates of the third and fourth tubes may be used to balance out the direct current components accurately. It is obviously necessary to use separate filament transformers for the third and fourth tubes.

The instrument as described is readily portable and has proved sufficiently reliable to yield continuous records of many hours' duration without an attendant. It is not a precise instrument for detailed analysis of wave form, but it is convenient and cheap in operation and yields records such as those presented in another paper,[6] which we believe are of great practical and theoretical significance.

6. Gibbs, F. A.; Davis, H., and Lennox, W. G.: The Electroencephalogram in Epilepsy and in Conditions of Impaired Consciousness, Arch. Neurol. & Psychiat., this issue, p. 1133.

COUGHING: A METHOD OF REENFORCING THE KNEE JERK REFLEX

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It is commonly known that frequently the patellar reflex cannot be obtained unless some special maneuver is employed to elicit it. The most usual means of reenforcing the knee jerk is the Jendrassik technic.[1] By this method the patient is instructed to flex partially the fingers of each hand, to place the palmar surface of the flexed fingers of one hand against the palmar surface of the flexed fingers of the other hand and at the command of the physician to pull hard with the fingers of one hand on those of the other. As the patient thus pulls, the examiner taps the patellar tendon. By this procedure the amplitude of the reflex is usually increased, or a reflex which could not be secured by tapping the tendon alone is obtained. The reason for the success of the reenforcement maneuver is that as a result of it the attention of the patient is no longer concentrated on his knee and leg, so that as he pulls with one hand on the other, the leg, which previously had been held stiff and rigid, now hangs relaxed and is in a perfect state for the reflex to be tested. Thus cerebral inhibition of the reflex is removed. Moreover, as Sherrington[2] showed, the cerebral and subcerebral activity involved in going through the Jendrassik procedure results in an overflow of stimuli to the reflex arc of the knee jerk and in a consequent reenforcement of that reflex.

Although many other methods of reenforcing the patellar reflex have been employed, varying from taking a deep breath or talking[3] to listening to Beethoven's Funeral March[4] the most commonly employed method is that of Jendrassik.

Three years ago it occurred to me that the easiest way to distract a patient's attention and reenforce the knee jerk reflex would be to have him gaze at the ceiling and at command to cough, and just as he coughs to have the examiner tap the patellar tendon. I have found this method simple and efficient. Its advantages over the Jendrassik technic are: 1. It is easier for the patient to understand the instruction to cough than it is to understand that of the Jendrassik procedure. 2. The attention of the patient is more easily distracted from his leg by the cough than by the Jendrassik maneuver, for often, even though the patient pulls with one hand on the other, he pays attention to his leg. Almost never, however, will a patient continue to think of his leg at the moment that he is coughing. 3. It enables the physician to tap the tendon at the most advantageous moment, for he need only wait for the patient to cough and during the coughing tap the tendon. On the other hand, the best moment for tapping the tendon in

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From the Meyer A. Rabinowitz Medical Service of the Jewish Hospital.

1. Jendrassik, E.: Zur Untersuchungsmethode des Kniephaenomens, Neurol. Centralbl. **4**:412, 1885.

2. Sherrington, C. S.: The Integrative Action of the Nervous System, New Haven, Conn., Yale University Press, 1923, p. 175.

3. Mitchell, S. W., and Lewis, M. J.: Physiological Studies of the Knee-Jerk and of the Reactions of Muscles Under Mechanical and Other Excitants, M. News **48**:169 and 198, 1886.

4. Lombard, W. P.: The Variations of the Normal Knee-Jerk and Their Relation to the Activity of the Central Nervous System, Am. J. Psychol. **1**:5, 1887.

the Jendrassik method is that at which the patient is pulling his hardest. This moment is somewhat difficult to determine.

By employing the coughing procedure I have been able to obtain the reflex readily when it has been difficult or even impossible to obtain it with the Jendrassik maneuver.

In making a search of the literature on the patellar reflex, I lately found that Popper [5] in 1920 suggested the employment of coughing as a method of reenforcement. I found, however, no mention of this method of reenforcement in the entire medical literature published in the English language, in textbooks, special articles or abstracts appearing in neurologic journals; even in German, in which Popper's article appeared, there has since been no mention of this means of reenforcement.

It has seemed to me therefore worth while to confirm the value of this simple and efficacious method of reenforcing the knee jerk and to bring it to the attention of physicians in America.

SUMMARY

The value of the Popper method of reenforcing the knee jerk is confirmed.

5. Popper, E.: Zur Kenntnis des Patellarreflexes, zugleich über eine neue Methode der Reflexverstärkung, Deutsche Ztschr. f. Nervenh. **67**:131, 1920.

SILVER CELLS (STEINER'S METHOD) IN MULTIPLE SCLEROSIS COMPARED WITH THEIR PRESENCE IN OTHER DISEASES

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Steiner's [1] contention that spirochetes may be found in the brain tissue of patients with multiple sclerosis has been viewed generally with considerable skepticism. Using the method described in his monograph, we have searched for spirochetes and silver cells alike, since Steiner claimed that only in the tissues of persons with a spirochetal disease are silver cells present. Rogers [2] found silver cells in the brain tissue of eleven patients with disseminated sclerosis but none in the brain tissue of four patients with other diseases. Following this lead we examined tissue from the brains of eleven patients with multiple sclerosis (and one other with a borderline case), of two patients with dementia paralytica and of fifty-one patients with various disease conditions.

Blocks of tissue were cut from the white matter contiguous to the right and the left lateral ventricle and whenever possible from the fourth ventricle. Three stained, mounted specimens from each of the three ventricles were examined.

Silver cells were seen in the brain tissue of ten of the eleven persons with undoubted multiple sclerosis. The cells occurred in greatest number in or around the walls of blood vessels. In the tissue of the patient with the borderline case, in which the pathologic diagnosis lay between diffuse sclerosis and acute multiple sclerosis, a single silver cell was noted. Silver cells were not observed in the spinal cord (the only tissue examined) of a patient who supposedly had multiple sclerosis. Silver cells and spirochetes were noted in the brain tissue of the two patients with dementia paralytica used as controls.

In the brain tissue of 5 of the patients with multiple sclerosis a few silver-stained bodies appeared which might be interpreted as being degenerated forms of spirochetes, but clearly defined spirochetes could not be found. We prefer to leave open the question of the incidence of spirochetes in cases of multiple sclerosis until we have had an opportunity to examine fresher material.

The search for silver cells in the tissue of patients with other diseases was conducted in the same manner as that in the tissue of patients with multiple sclerosis, except that the diagnosis remained unknown to the observer until the examination was completed. The clinical diagnoses and the number of cases of each condition in which tissue was examined were: Alzheimer's disease, 1; amaurotic idiocy (juvenile), 1; anterior poliomyelitis, 1; arteriosclerosis, 5; arteriosclerosis (with softening), 1; tumor of the brain, 3; cerebral syphilis, 2; chronic alcoholism, 1; congenital syphilis (juvenile), 1; dementia praecox, 3; diffuse sclerosis (pathologic diagnosis), 1; epidemic encephalitis, 3; epilepsy, 1; Friedreich's

From the Department of Bacteriology, New York State Psychiatric Institute and Hospital.

1. Steiner, G.: Krankheitserreger und Gewebsbefund bei multipler Sklerose, Berlin, Julius Springer, 1931; Neues zur Aetiologie der multiplen Sklerose, Nervenarzt **5**:281, 1932.

2. Rogers, H. J.: The Question of Silver Cells as Proof of the Spirochaetal Theory of Disseminated Sclerosis, J. Neurol. & Psychopath. **13**:50, 1932.

ataxia, 1; dementia paralytica, 1; Huntington's chorea, 1; idiocy, 1; involutional melancholia, 1; involutional melancholia, with pellagra, 1; intestinal obstruction (toxemia), 1; lead poisoning, 1; lobar pneumonia, 1; meningitis, 1; multiple sclerosis (no plaque included), 1; normal (violent death), 3; ophthalmoneuromyelopathy, 1; Parkinson's disease, 1; peritonitis, 1; Pick's atrophy, 1; Raynaud's disease (with epilepsy), 1; septicemia, 1; tetanus, 1; tuberculous meningitis, 2; tuberous sclerosis, 2, and typhoid, 1.

In the tissues of only one brain in the control series were silver cells seen, viz., in that of a patient with congenital syphilis. Numerous spirochetes were likewise demonstrated in this specimen. It will be noted that in the control series the brain of a patient with dementia paralytica and one of a patient with multiple sclerosis were included. The latter happened to be the only one in which silver cells were not noted among the brains of the 11 patients with multiple sclerosis originally examined.

Steiner's conclusions concerning the presence of silver cells in the tissue of patients with spirochetal diseases and their absence in the brain tissue of other persons are therefore confirmed. In studies of this nature positive results are convincing; negative conclusions leave something to be desired. Our failure to observe silver cells in the brain of one patient with multiple sclerosis and in one with dementia paralytica raises the question whether the examination of nine slides per brain is adequate. Rather than continue the examination of the brains of patients with multiple sclerosis, in which silver cells were not noted, we prefer to leave the matter as it stands—on a strictly comparative basis.

SUMMARY

Silver cells were present in the brains of ten of eleven patients with multiple sclerosis examined by the Steiner method.

In five of the brains showing silver cells, stained bodies were observed which were suggestive, but not conclusively indicative, of spirochetes.

Of a miscellaneous collection of fifty-one brains studied in an identical manner, only one revealed silver cells—that of a child with congenital syphilis.

SPECIAL ARTICLES

SIR CHARLES SHERRINGTON

ARTHUR R. ELVIDGE, M.D.
AND
WILDER PENFIELD, M.D.
MONTREAL, CANADA

The work of so great a physiologist as Sir Charles Sherrington may be described and appreciated, but it would be presumptuous for his contemporaries to attempt the final assessment of its value. In outlining his discoveries it becomes apparent at once that in general they form one structure from a well laid foundation to crowning conclusions. Like Hughlings Jackson he has penetrated always to the underlying principles of neurology, but unlike Jackson he has been able to prove each step of his work and to verify each hypothesis.

EARLY YEARS

Charles Scott Sherrington, son of James Sherrington, of Yarmouth, was born in London on Nov. 27, 1857. His father died early, so that Charles and his brothers were bound to their mother by a double bond of affection. She was married a second time, and the stepfather, Dr. Caleb Rose, son of Caleb Burrell Rose,[1] is responsible for many of the early preoccupations of the boys. While the children were still young the family moved to Ipswich, at that time a center for those interested in geology and archeology. This, together with the fondness of his stepfather for these subjects, roused in Charles a lasting interest in the whole field. He was educated at Queen Elizabeth's School, Ipswich, with his two younger brothers, W. S. Sherrington, who became a barrister and died in 1918, and G. S. Sherrington, a solicitor. It is said that the barrister was the most brilliant of the three in his school work, while the other two excelled in athletics at this time.

At Ipswich Charles seems to have been particularly influenced by a master named Thomas Ashe, a scholar who had published some fine

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From the Montreal Neurological Institute.

Such words as "physiologic" and "neurologic" are used in this article only in order to comform to the nomenclature which is compulsory for publication in the ARCHIVES. The authors would prefer the words "physiological," "neurological," etc.

1. The Dictionary of National Biography, edited by Leslie Stephen and Sidney Lee, New York, Oxford University Press, 1908.

verse; from him he evidently learned the art of poetic expression, and he developed considerable skill in classical composition. Furthermore, in his own home was to be found a high standard of culture, and the family possessed an unusual collection of fine paintings. It is hardly surprising in view of the penetrating mind and retentive memory of Sir Charles that amid such boyhood influences he developed a continuing interest in geology, archeology, the classics and painting.

Deciding on a career of medicine, he matriculated in 1881 at Cambridge and was admitted to Gonville and Caius College. In the study of physiology he came under the influence and tutelage of Sir Michael Foster, who had a way of selecting his pupils and encouraging them along those avenues of research best suited to their talent. Foster, in the words of Sharpey-Schafer,[2] "would make the bones of biological science, which were becoming very dry at Cambridge, live again." He had created a very active physiologic department, gathering about him such men as Balfour, Gaskell, Langley, Newell Martin, Sheridan Lea and others.

Amid this stimulating environment Sherrington engaged in research even during his undergraduate years, and his first short paper, recording a demonstration before the Physiological Society, written in association with Langley,[3] was entitled "On Sections of the Right Half of the Medulla Oblongata and of the Spinal Cord of the Dog Which was Exhibited by Professor Goltz at the International Medical Congress of 1881." His second publication, also written in collaboration with Langley,[4] was entitled "Secondary Degeneration of Nerve Tracts Following Removal of the Cortex of the Cerebrum in the Dog."

This early work under the influence and guidance of Foster and in association with Langley, who was five years his senior, instilled into Sherrington an interest in neurophysiology from which he never escaped, although his first intention was to make pathology his life work. But this research did not encroach too greatly on his undergraduate studies, for he took his examinations in physiology in two of the tripos with distinction and was awarded the Shuttleworth Scholarship in 1883. The following year he obtained the degree of Bachelor of Arts and was elected George Henry Lewes Student.

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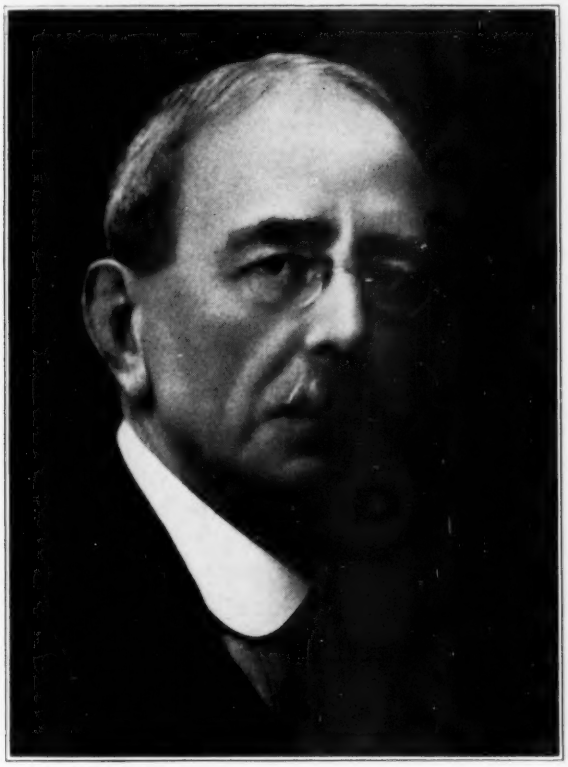
2. Sharpey-Schafer, Edward: History of the Physiological Society During Its First Fifty Years, 1876-1926, London, Cambridge University Press, 1927.

3. Sherrington, Charles, and Langley, J. N.: On Sections of the Right Half of the Medulla Oblongata and of the Spinal Cord of the Dog Which Was Exhibited by Professor Goltz at the International Medical Congress of 1881, J. Physiol. **5**:6 (Proc.), 1884.

4. Langley, J. N., and Sherrington, Charles: Secondary Degeneration of Nerve Tracts Following Removal of the Cortex of the Cerebrum in the Dog, J. Physiol. **5**:49, 1884.

In 1885 he secured his degree in medicine (M.B.) from Cambridge and accompanied C. S. Roy to Spain to assist in a study of cholera in that country. Roy, who had probably influenced him in the first place to take up pathology, had himself been appointed to the chair of pathology at Cambridge at the early age of 30. The following year Sherrington visited Italy alone, apparently to continue this study of cholera, and he relates how he once performed a most important autopsy in a small town in spite of threats from the excited populace.



SIR CHARLES SHERRINGTON

From Italy Sherrington carried his pathologic material to Berlin, where he settled down to cut sections in the laboratory of the great Virchow. Here, however, he met with disappointment, for he had come at a time when the famous pathologist was chiefly interested in politics. At the end of two apparently unsatisfactory months in this laboratory Virchow looked over his work and sent him to Koch's laboratory, where he took the prescribed six week preliminary course in technic and stayed nearly a year. In 1887 he was awarded the Thurston prize at Cambridge and was elected a fellow of his college.

On returning to London, Sherrington was made lecturer in physiology at St. Thomas's Hospital, and in 1891 he was appointed professor superintendent of the Brown Institute for Advanced Physiological and Pathological Research. In this post he succeeded Sir Victor Horsley, whose early investigative work in neurophysiology had been done in that institute. This gave Sherrington a splendid opportunity for animal experimentation, and it was during his first year here that on learning of Behring's antitoxic serum he prepared the serum himself and used it successfully about three years before it was accepted in England.

In 1891 he married Ethel Mary Wright, daughter of John Ely Wright, of Preston, Suffolk. She was a high-spirited girl, a great enthusiast for sports and a sympathetic companion. They had one child, Carr E. R. Sherrington, born in 1897, who is now a distinguished railroad economist and author.

Between 1885 and 1895 Sherrington made several visits to Strasbourg to study under the physiologist Goltz, whose chief interest lay in the function of the central nervous system, and it is said that Sherrington made an effort to induce Goltz to accept or to test the work of Ferrier on central localization, but without success. Nevertheless, Sherrington's interest in pathology by no means waned, as is shown by many of his subsequent papers.[5] Most of his researches were in the field of physiology, and the majority of his publications already bore some direct connection with the nervous system. Those in other fields decreased in number but never disappeared, even in later years. His earliest work on the nervous system and a large proportion of his later work concerned degeneration of the ascending and descending nerve tracts in the spinal cord following cerebral lesions and section of the spinal nerve roots. This work not only confirmed much of what was then known about neuro-anatomic pathways but cast light on the physiology of these pathways. In 1893, at the age of 36, he was elected a Fellow of the Royal Society.

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5. Roy, C. S.; Brown, J. Graham, and Sherrington, Charles: Preliminary Report on the Pathology of Cholera Asiatica, as Observed in Spain, 1885, Proc. Roy. Soc., London **41**:173, 1886. Sherrington, Charles: Note on the Anatomy of Asiatic Cholera as Exemplified in Cases Occurring in Italy in 1886, ibid. **42**:474, 1887. Sherrington, Charles, and Ballance, C. A.: On Formation of Scar Tissue, J. Physiol. **10**:550, 1889. Sherrington, Charles, and Hadden, W. B.: The Pathological Anatomy of a Case of Locomotor Ataxy with Special Reference to Ascending Degenerations in the Spinal Cord and Medulla Oblongata, Brain **11**:325, 1889. Sherrington, Charles: Note on Some Changes in the Blood of the General Circulation Consequent upon Certain Inflammations of an Acute Local Character, Proc. Roy. Soc., London **54**:487, 1893-1894; **55**:161, 1894; Experiments on the Escape of Bacteria with the Secretions, J. Path. & Bact. **1**:258, 1892-1893; Varieties of Leucocytes, Science Prog. **2**:415, 1895.

During this period before 1895 many minor contributions appeared on a variety of topics connected with neurophysiology, too numerous to mention in detail. They included studies on the optic nerve of the rabbit, ocular movements, ganglion cells in the mammalian spinal cord, pilomotor nerves, the cervical portion of the sympathetic system of the monkey, the nerve supply to the bladder and anus, the knee jerk, dichotomous branching of the medullated fibers in the brain and spinal cord, the correlation of the action of antagonistic muscles, the anatomic constitution of muscle nerves and comments on recurrent fibers in the ventral roots and on the influence of sensory nerves on movement and the nutrition of the limbs.

As early as 1892 Sherrington had published work on the localization of the knee jerk, the spinal nuclei of the pelvic limb muscles, the arrangement of motor fibers in the lumbosacral plexus and the peripheral distribution of posterior roots. Further work on the spinal nerve roots followed at intervals, until he was eventually able to outline completely the whole somatic sensorimotor segmental innervation for the monkey. This investigation of the distribution of the nerve roots is a splendid example of his thoroughness and persistence in research, for it was all carried out, to use his own words, "as a step preliminary to observations on the reflex functions of the spinal cord." [6] This work was to explain many intricate mechanisms involved in the physiology of the spinal cord and eventually to give the present day conception of spinal reflex phenomena.

Many points of first importance were investigated incidentally in the course of this great work. Spinal shock was first described and thoroughly investigated in the monkey, amplifying the scant knowledge already current regarding this condition in dogs. The laws observed in spinal reflex action, such as had been stated by Pflüger, were elaborated and corrected. The inhibition described by Goltz in spinal reflexes was investigated. The correlation of action of antagonistic muscles was noted and studied, and this led to Sherrington's coining the term "reciprocal innervation," perhaps borrowed from the term "reciprocal action" [7] used in connection with visual phenomena by William Baly.[8] Finally Sherrington summarized much of his work on spinal reflexes in 1897 in the Croonian Lecture entitled "The Mammalian Spinal Cord as an Organ of Reflex Action," and two years later in the Marshall Hall prize address, "On the Spinal Animal."

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6. Sherrington, Charles: Experiments in Examination of the Peripheral Distribution of the Fibers of the Posterior Roots of Some Spinal Nerves: II, Phil. Tr., London (sect. 4) **190B**:128, 1898.

7. Sherrington, Charles: On Reciprocal Action in the Retina as Studied by Means of Some Rotating Discs, J. Physiol. **21**:33, 1897.

8. Müller, J.: Elements of Physiology, translated from the German with notes by William Baly, London, Taylor & Walton, 1842, vol. 2, p. 1185.

THE LIVERPOOL PERIOD

In 1895 Sherrington accepted the chair of physiology in the University of Liverpool and moved to that city for what proved to be eighteen years of uninterrupted work in his chosen field. A number of papers appeared each year recording advances of first importance in regard to the more detailed analysis of neuromuscular phenomena in the mammal, many of which concerned the significance of proprioceptive innervation of muscles and "reciprocal innervation" of antagonistic muscles. Between 1896 and 1898 he described decerebrate rigidity, and in 1904 published "The Correlation of Reflexes and the Principle of the Common Path."[9] In 1905 he delivered the Silliman Lectures at Yale, which appeared in book form under the title "The Integrative Action of the Nervous System."[10] This careful analysis of his observations on spinal reflex phenomena, laws of conduction and inhibition, innervation of the skin and muscles and the physiology of the spinal cord in general demonstrated that through his exhaustive studies he had built up constructive hypotheses and gradually converted them into accepted physiologic principles. So complete a demonstration was it that these principles became simple and obvious, which is the final test of logical reasoning.

But this period was not by any means entirely devoted to the problems of the physiology of the spinal cord. New research was undertaken which led to important discoveries in the physiology of the cerebral cortex and in cerebral localization. Sherrington managed to secure some anthropoid apes, chimpanzees and orang-utans and even two gorillas for this work. A number of years earlier Horsley and Beevor[11] had concluded from a study of a single available orang-utan's brain that the gyrus postcentralis was excitable, this evidence of excitability having been obtained at two points only. This was the first time that the brain of an anthropoid had been studied by electrical stimulation. However, Sherrington and Grünbaum,[12] using weak unipolar stimulation, found the postcentral gyrus in the anthropoid to be inexcitable to a stimulus which evoked a response from the precentral gyrus but which facilitated elicitation of movement from the latter.

Many other problems of a neurophysiologic character were investigated: the physiology of sensation in the retina, the peripheral dis-

9. Sherrington, Charles: The Correlation of Reflexes and the Principle of the Common Path, Rep. Brit. A. Adv. Sc., 1904, p. 728.

10. Sherrington, Charles: The Integrative Action of the Nervous System, New Haven, Conn., Yale University Press, 1906.

11. Paget, Stephen: Sir Victor Horsley: A Study of His Life and Work, London, Constable & Co., Ltd., 1919, p. 110.

12. Sherrington, Charles, and Grünbaum, A. S.: Observations on the Physiology of the Cerebral Cortex of the Anthropoid Apes, Proc. Roy. Soc., London **71**:58, 1903.

tribution of fibers in the posterior roots, the physiology of reflex action, the anatomy of the dorsal roots, decerebrate rigidity and reflex coordination of movement, sensory nerves to ocular muscles, the value of vascular and visceral factors for the genesis of emotion and the dorsal spinocerebellar tract. Further, Sherrington described investigations of plastic tonus, proprioceptive reflexes, the pilomotor system and the "mammalian spinal preparations" which recall the frog spinal preparation of Goltz. These scientific papers did not prevent Sherrington from writing on more general topics, some of which were of a public health nature.[13] In addition, he had written large sections on the nervous system for Schäfer's "Text-Book of Physiology" (1900) and for Foster's "A Text-Book of Physiology" (seventh edition, 1897), articles on cardiac physics for Allbutt's "System of Medicine" (1898) and on the general anatomy and physiology of the nervous system for Allchin's "Manual of Medicine," chapters for the "Encyclopaedia Britannica" and several chapters in "A Manual of School Hygiene" by E. W. Hope, E. A. Brown and C. S. Sherrington (1913).

OXFORD PERIOD

With so much accomplished and after such long sustained research, Sherrington must have welcomed the comparative quiet of Oxford, the small classes of students, the short terms and the beauty of town and river. He has expressed his feeling for the university's setting in verse that demonstrates another luminous facet in the personality of a great scientist:

> The night is fallen and still thou speakst to me,
> What though with one voice sole, with accents many,
> Tongued turret and tongued stream, tracked pasture fenny,
> And cloister spirit trod, and centuried tree,
>
> . . .
>
> Sworn Priest of Beauty, these thy shrines among,
> That kneelst with old folk and that dancest with young.

13. Sherrington, Charles; Boyce, R., and Ross, R.: The History of the Discovery of Trypanosomes in Man, Lancet **2**:1426, 1902. Sherrington, Charles: The Name of the Red Corpuscle: A Suggestion, Brit. M. J. **1**:742, 1901. Roaf, H. E., and Sherrington, Charles: Experiments in Examination of the "Locked Jaw" Induced by Tetanus-Toxin, J. Physiol. **34**:315, 1906. Sherrington, Charles: Observations with Anti-Tetanus Serum in the Monkey, Lancet **2**:964, 1917. Sherrington, Charles, and Sowton, S. C. M.: On the Dosage of the Isolated Mammalian Heart by Chloroform, Brit. M. J. **2**:162 and 721, 1904; On the Dosage of the Mammalian Heart by Chloroform, Arch. di fisiol. **2**:140, 1904; The Effect of Chloroform on the Heart, Rep. Brit. A. Adv. Sc., 1904, p. 761; On the Relative Effects of Chloroform upon the Heart and upon Other Muscular Organs, Brit. M. J. **2**:181, 1905; On the Effect of Chloroform in Conjunction with Carbonic Dioxide on Cardiac and Other Muscles, ibid. **2**:85, 1906; Chloroform and Reversal of Reflex Effect, J. Physiol. **42**:383, 1911.

To the friendly doorway of his new house a pathway was soon beaten by students and graduate workers who found the hospitality of Lady Sherrington an unfailing joy. At her death (1933) Sir Charles lost an ideal helpmate, and his pupils, a rare friend. The Sunday afternoon teas, like those at the home of Lady Osler nearby in Norham Gardens, became for those fortunate enough to win Lady Sherrington's favor a cherished privilege. It is at such times as these that his pupils discover Sherrington to be a graceful host and a conversationalist of rare charm on many subjects far removed from physiology. His extraordinary memory makes it possible for him to "take into camp" the unsuspecting tutor of English in a discussion of the literature of some particular period or to hold a mixed company spellbound while he relates a humorous adventure or a tale of travel.

It was a short bicycle ride from their house at 9 Chadlington Road to the professor's laboratory. There was easy access to the Cherwell, where the Sherringtons, father, mother and son, loved the simple pleasures of boating. Sherrington became a Fellow of Magdalen and sometimes dined in that college, chatting late in the common room. It was during this Oxford period that he was knighted (1922), and further received that highest of all honors for an English savant, the presidency of the Royal Society, in 1920.

But the war years were at hand. His only son, just ready for Cambridge, was to be called into service, and years of anxiety for his safety followed. Sherrington's book of poems, "The Assaying of Brabantius and Other Verse," which appeared in 1925, was tempered to some extent at least by war sentiment. Another great neurologist and close friend of Sherrington, Sir Henry Head, who also turned his talent to poetry under the stress and strain of war time, has well expressed how hard it was for those who were "too old to fight":

> How can I serve who am too old to fight?
> I can not stand and wait
> With folded hands, and lay me down at night
> In restless expectation that the day
> Will bring some stroke of Fate
> I cannot help to stay.
> Once, like a spider in his patterned web,
> Based on immutable law,
> Boldly I spun the strands of arduous thought,
> Now seeming naught,
> Rent in the sudden hurricane of war.

A letter written by Sherrington to his former pupil Alexander Forbes gives insight into this period, and excerpts [14] may be quoted

14. Atlantic Monthly, Oct., 1916, p. 544.

describing his work in a munitions factory, where he calls himself an unskilled laborer!

> This war absorbs all energies and persons here. . . . The change is enormous, as if, in a space of eighteen months, a generation's period had passed through. As a small instance, B. Shaw's plays, that claimed to be the intellectual novelties of their day, are dead; Bergson spoke of them in London the other day as no longer readable, as of "une mode démodée, une affectation passée." Certainly they would bore every one now, and it is difficult to trace in what their interest ever lay, so tedious they are become. . . .
>
> As for me, I am feeling the remoteness of my work from the great practical effort now in hand. . . . After the laboratory work is done I give my time to "helping" at the hospital. I should have liked to enter R.A.M.C., but consulted the University's wishes: these were that for the present I should stick to the Laboratory, which is of course frightfully short-handed, as the assistants have practically all gone into the army. In the summer the shortage of labour for "munitions" led me to get taken on as a workman (unskilled, of course) in a munitions factory at ——.
>
> It was a motor-car works in time of peace, but now converted into a 3-inch shrapnel shell factory. I was there three months, and it was getting more workers and machine-plant every week. Its output was 24,000 shells a week when I first went, and at the end, when I left, had risen to over 50,000. What it may be now, I do not know. They were working day and night without stop. I was on day-shift; the day-shift hours were 7.30 A. M. to 8.30 P. M. every week-day and 8 to 5 on Sundays. We had one hour for dinner (in a canteen, sixpence a head, plenty of fair food, but such table-cloths! Their only pattern was spots of spilled victuals!), and one half-hour for tea-supper at 5.30 (fourpence). We work-people were an odd assembly: some middle-aged, experienced workmen, old hands, sprinkled among the new ones to teach and to do the skilled processes; then, many hands from all sorts of steel trades but unskilled in this one; then many more, either very young or quite old, from various other than steel trades. . . .
>
> Our work was mainly gauging, and filling the shells and fitting on the fuse-sockets. Each shell contained 144 bullets and required over eighty separate "processes." ! . . .
>
> Our boy—now eighteen—is in the Third Battalion, Oxfordshire Light Infantry. I hope he will not be sent to the front until he is nineteen. He was to have gone up to Cambridge this October, to my old college, Caius. But he felt it his duty to give that up and enter the Service. He likes his comrades; many of them are University men. But the physical work and long hours of training, and exposure to weather are rather a strain at his age. However, he stands it well so far.

The production of scientific research not only for the actual period of the war but for several succeeding lean years had decreased. Few assistants and students remained. With each year, however, some contributions appeared to further Sherrington's studies on reflexes, cortical localization or other problems. The question of acoustic reflexes and postural activity began to be investigated (1909-1920), and as time went on the question of the stimulus and the physiology of the discharge mechanisms of the nervous impulse itself, rather than its effect,

came more and more to the front. The principle of "recruitment" was enunciated and studied.

In the more recent years, with a number of collaborators, a technic has been finally perfected for applying the knowledge hitherto gained on reflex phenomena to the study of the individual neuromotor unit. This most important work is continuing at the present time.

In the years following the war Sherrington was invited to give many formal addresses, among which were the inaugural address at the opening of the new Biological Building of McGill University and in 1927 the Dunham lectures at the Harvard Medical School.

At the beginning of his Oxford period the laboratory was cramped and the scientific budget inadequate. Having secured the most brilliant neurophysiologist in the world, the university allowed him to be burdened with an unfair weight of administration and with lack of assistance, "sharpening their pencils with a razor" after the habit of some universities. But gradually he wrought a change. The laboratory has now been rebuilt and reequipped. Graduate students clamor to work with him, and Sherrington has organized the teaching and developed his research to a new high level of activity and complexity.

His associates and pupils form an interesting list: in the first period of his scientific life, from 1884 to 1895, he wrote papers with J. N. Langley, C. S. Roy, J. Graham Brown, W. B. Hadden, C. A. Ballance and R. W. Reid; in the second period, from 1895 to 1913, with F. W. Mott, E. H. Hering, A. Fröhlich, A. S. F. Grünbaum, R. Boyce, R. Ross, E. E. Laslett, R. S. Woodworth, S. M. Sowton, H. E. Roaf, Frances M. Tozer, E. Schuster, J. Graham Brown and A. G. W. Owen; in the third period, since 1913, with E. W. Hope, E. A. Brown, A. Forbes, S. C. M. Sowton, F. R. Miller, A. S. F. Leyton, K. Sassa, E. G. T. Liddell, J. F. Fulton, R. S. Creed, S. Cooper, D. Denny-Brown and J. C. Eccles. His students are legion. Among his American pupils are H. C. Bazett, Stanley Cobb, Harvey Cushing, Alexander Forbes, John Fulton, Grayson McCouch, Wilder Penfield, Henry Viets, Lewis Weed and R. S. Woodworth. In addition, he has trained many physiologists from various parts of the world, and his method of practical laboratory training with mammals is a distinct advance in the medical curriculum now in general use.

During his career the honors which have come to him are too numerous to mention: membership in European scientific societies and academies, honorary degrees and gold medals and prizes both at home and abroad. In 1932 he and Professor Adrian of Cambridge received the Nobel award for medical research, which they divided, as Cajal and Golgi had done in 1906.

Sherrington's scientific contributions show clarity of thought and the accuracy of record and observation which are essential in this type

of work. He is an untiring experimenter, careful, self-critical, gratefully appreciative of the work of others and never in a hurry to publish his results. Experiments dated 1887 did not appear in print until 1893.

To quote his Cambridge colleague, Professor Adrian:[15]

> The general principles of reflex action which Sherrington has formulated have had an immediate practical application to the problems of nervous disease and experimental psychology, and it is no exaggeration to say his researches have opened up an entirely new chapter in the physiology of the central nervous system.

To his life's work he has brought the rare combination of ability for exhaustive experimentation and restrained integrative generalization. This year he retires from his teaching position at Oxford at the height of his power and with no serious opponents or critics in the scientific world. Neurologists gathered at Bern in 1931 for their first International Congress singled him out for special honor, and their spokesman, Professor Asher, referred to him with true insight as "the philosopher of the nervous system."[16]

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15. Adrian, E. D.: Professor Sherrington's Work on the Nervous System, Nature, London **106**:442, 1920.

16. Fulton, John: The Nobel Prize in Physiology and Medicine, Sir Charles Scott Sherrington, Scient. Monthly **35**:568, 1932.

News and Comment

SCIENTIFIC EXHIBIT, KANSAS CITY, MO.

Application blanks for space in the scientific exhibit at the Kansas City session of the American Medical Association are now available. The Committee on Scientific Exhibit requires that all applicants fill out the regular form. Applications close on Jan. 27, 1936. The representative of the Section on Nervous and Mental Diseases to the Scientific Exhibit is Dr. Peter Bassoe, 8 South Michigan Avenue, Chicago. Application blanks may be obtained from Dr. Bassoe or from the Director, Scientific Exhibit, 535 North Dearborn Street, Chicago.

REORGANIZATION OF THE INTERNATIONAL LEAGUE AGAINST EPILEPSY

At the time of the International Neurological Congress in London a meeting of those particularly interested in epilepsy was held on July 31, 1935, at the Lingfield colony. Thirty-two physicians representing fourteen countries were present. After discussion it was unanimously decided that the International League Against Epilepsy should be revived and that the immediate efforts should be directed toward the improvement of the social condition and the institutional care of persons with epilepsy. To this end it was agreed that there should be a publication, issued annually or oftener, acquainting readers with the facilities and the remedial efforts in various countries. Plans were also laid for a meeting of the league at the time of the next Neurological Congress in Copenhagen.

At an adjourned meeting, held on August 2 (Prof. A. Ley of Brussels in the chair), the following officers were elected: president, William G. Lennox, Boston; secretaries, H. I. Schou, Filadelfia, Denmark, and L. J. J. Muskens, Amsterdam, Holland; treasurer, J. Tylor Fox, Lingfield, Surrey, England.

All persons interested in improving the condition of epileptic patients are invited to join the league.

ASSOCIATION FOR RESEARCH IN NERVOUS AND MENTAL DISEASE

The annual meeting of the Association for Research in Nervous and Mental Disease will be held on Dec. 27 and 28, 1935, at the Waldorf-Astoria Hotel, Park Avenue and Fiftieth Street, New York. The subject of the meeting will be "Tumors of the Nervous System."

Obituaries

GEORGE HUGHES KIRBY

1875-1935

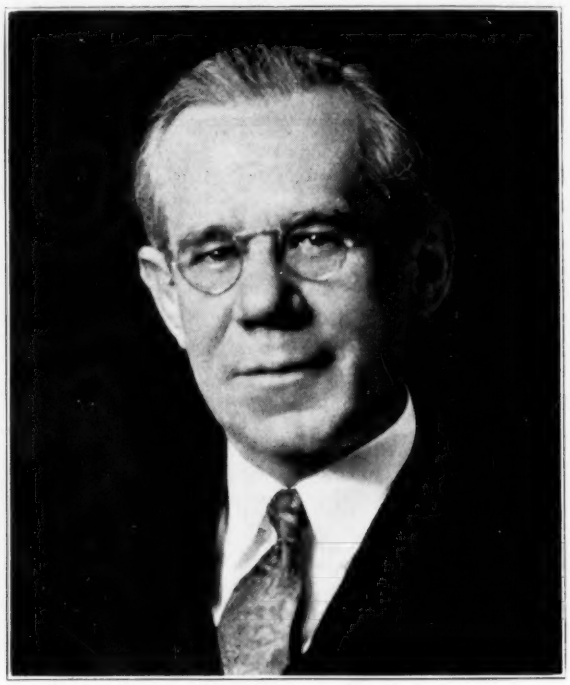
Dr. George Kirby, who died suddenly on Aug. 11, 1935, was rightly considered one of the pioneers of modern American psychiatry. Most of his professional life was spent in the service of the New York state hospitals, and he brought to that service ideals of scientific honesty and thoroughness of psychiatric investigation and treatment that did much to improve the service in hospitals for patients with mental disease not only in his own state but throughout the country.

Dr. Kirby was born in Goldsboro, N. C., on Feb. 9, 1875. He was graduated from the University of North Carolina in 1896 and from the Long Island College Hospital in 1899. Immediately he went into his chosen field of psychiatry, and from 1899 to 1902 he served on the staff of the Worcester State Hospital in Massachusetts as assistant physician. On leaving Worcester in 1902 he went to the New York State Psychiatric Institute on Ward's Island as associate in clinical psychiatry. In 1908, when the position of director of clinical psychiatry was established in the New York state hospitals, Dr. Kirby was appointed to the first post at the Manhattan State Hospital on Ward's Island. The establishment of this position was an attempt to improve the scientific work in the state hospitals, and the choice of Dr. Kirby for this post was a happy one, for in him were combined the scientific ideals and the kindly diplomacy that were necessary to establish the position as the valuable one it has since proved to be. For a few months in 1917 Dr. Kirby served as medical inspector of the New York State Hospital Commission, and in October of that year he was appointed director of New York State Psychiatric Institute, succeeding Dr. August Hoch.

Directing a large scientific psychiatric institute was the sort of thing Dr. Kirby did best, and it was the good fortune of the state of New York to have him at the head of its psychiatric institute during the important formative years of that valuable institution. During his term of office he saw his institute expand from ancient, cramped quarters on Ward's Island to its present fine building at the Columbia-Presbyterian Medical Center. It was under his guidance that his organization ceased to be a restricted one in the service of the New York state hospitals and became an important department in the Medical School of Columbia University. In this work he carried on until poor

health forced his resignation in 1931, and from this time until his death he was in private practice in New York.

During all these years Dr. Kirby did not restrict himself to the service of the New York state hospitals. He was an inspiring teacher, and for over twenty years he devoted considerable time to the teaching of psychiatry. From 1914 to 1919 he was professor of psychiatry in New York University and Bellevue Hospital Medical College; from 1917 to 1927, professor of psychiatry in Cornell University Medical College, and from 1927 to 1932, professor of psychiatry in the College



GEORGE HUGHES KIRBY
1875-1935

of Physicians and Surgeons (Columbia University). After resigning from Columbia, he returned to the psychiatry department at Cornell, where he taught until his death in the position of professor of clinical psychiatry.

In July 1918, Dr. Kirby was commissioned a major in the medical corps of the United States Army and served first on the staff of the surgeon of the Port of Embarkation, New York, and later on the staff of United States Hospital No. 1 and of special units until his discharge from the army in March 1919. His membership in medical and other

scientific societies was varied and extensive. He served as president of the American Psychiatric Association, the New York Neurological Society and the New York Psychiatric Society and as the first president of the New York Society for Clinical Psychiatry. In 1919 he was elected to fellowship in the American Neurological Association. In 1929 he received the signal honor of the degree of LL.D. from his Alma Mater, the University of North Carolina.

Dr. Kirby was a gentle person who showed impatience only with dishonesty. Of the strictest personal scientific honesty himself, he was intolerant of anything else. He lived through the years of formation of modern American psychiatry, and he was one of those who helped to give form to it by his writing and his teaching. Never radical and never really conservative, he lived and taught a psychiatry that was always in close touch with human realities. Always keenly conscious of the other person's point of view, he felt deeply and suffered not a little, and these are the qualities that make the sort of friend that George Kirby was to those who worked with him.

LOUIS CASAMAJOR, M.D.

Abstracts from Current Literature

INDIVIDUAL DIFFERENCES IN NORMAL COLOUR VISION: A SURVEY OF RECENT EXPERIMENTAL WORK FROM 1910 TO 1931. W. O. PIERCE, Medical Research Council, Spec. Rep. Ser., no. 181, London, His Majesty's Stationery Office, 1933.

The preface of this publication contains the following statement: "Problems of colour vision have much practical importance in industry, as also in the work of various Government Departments and especially of the Defence Services, and this survey of existing knowledge was prepared with a specific purpose in view. This was to collect information as to differences in colour vision among 'colour normal' individuals, the object being the construction of tests for the selection and classification of workers on the basis of their colour sensitivity. The information is of much interest apart from this, and the Council is glad to have the opportunity of making it generally available."

There are seven subsections in this article. The first deals with discrimination of brilliance or luminosity, the second with discrimination of saturation, the third with chromatic sensibility, the fourth with differences in "after-excitation" phenomena, the fifth with differences in the color fields and the sixth with color anomalies. The seventh subsection contains a report on a group of other experiments on color vision, including photometric investigations, color and the visibility of objects and certain psychologic investigations connected with color vision.

The existence of individual differences in color discrimination has been known for a long time. The differences between persons with normal color vision and those who are color-blind have necessitated the construction of various tests for determining these differences in color discrimination. When under experimental conditions it is found that different subjects give significantly different results, these differences are reported as individual. The object of this survey was to study the type and magnitude of such individual differences. The scope of the survey is limited to such differences only between persons with normal color vision, except for a few investigations reported in section VI, in which the results obtained were either from mixed groups of persons with normal color vision and those who were color-blind or from large groups of persons who were color-blind.

For the purpose of this abstract the reviewer wishes to mention especially sections I and V and a portion of section VII. The entire work is most readable, and it is recommended that it be read in its entirety.

Brilliancy and saturation, so far as they play a rôle in colors, are two attributes not always well understood. The first of these is that attribute of any color in respect to which it may be classed as equivalent to one member of a series of grays. It can be specified numerically in terms of the difference which exists between it and black. Hue is that attribute of certain colors in respect to which they differ from a gray of the same brilliance. This attribute indicates a qualitative rather than a quantitative difference. Saturation is that attribute of all colors possessing a hue which determines their degree of difference from a gray of the same brilliance.

A few outstanding results of field studies follow: Under light adaptation with a foveal size field and at high intensity the eye shows the least response to change of intensity. 1. Chromatic sensitivity of all wavelengths falls off from the center of the field to the periphery, e. g., yellow 276—275, 170 times less; green 400—420, 443 times less; blue 659—653, 298 times less; red 728—724, 885 times less, depending on the quadrant studied. Great irregularities occurred in the ratio of sensitivity from point to point for a given color in the same meridian quadrant and at corresponding points in different quadrants. Small regions of decreased sensitivity to one color, in some cases amounting to almost complete color-blindness, were found, but with no loss of sensitivity for most other colors. 2. The distribution of

the color fields was found to vary with the energy of the stimulus used; much interlacing and criss-crossing of limits were found for red, blue and green. In general, the area of a color field varied with the logarithm of the intensity of the light. On the basis of some of the experimental findings, the author thinks that the nerve endings of the rods and cones in the retina are barely connective and that they have nothing to do with the discrimination of color. [This is interesting in view of Henchen's opinions as to color perception.] Pierce believes that in the investigation of the colors as they appear in the peripheral portion of the retina that there is a strong central or cerebral element to be considered. In his opinion the following factors are of great importance in the investigation of the color fields: (*a*) brightness of preexposure and surrounding field; (*b*) intensity of general illumination; (*c*) time of exposure of stimulus; (*d*) size of stimulus; (*e*) purity of stimulus; (*f*) brightness of stimulus (not important for pigments); (*g*) intensity of stimulus (very important). Especially was the author impressed with two findings under conditions of light adaptation. He concurs in Oeser's findings and opinions. The difference in form and color perception is related to a difference in psychophysiologic make-up. Form and color as selective principles in perception can, therefore, function independently in different persons both at lower and at higher levels.

The larger the field investigated, the greater is the precision of color temperature matching. The nearer the fields, the greater the precision. A dividing band of black when comparing the results obtained from right and left in both eyes gives poorer results than a band of the same color as the color temperature.

The few findings quoted are more or less disconnected, but also they are outstanding and should stimulate close interest for a careful reading of the complete work.

SPAETH, Philadelphia.

MÉNIÈRE'S DISEASE: SYMPTOMS, OBJECTIVE FINDINGS AND TREATMENT IN FORTY-TWO CASES. WALTER E. DANDY, Arch. Otolaryng. **20**:1 (July) 1934.

Dandy practices hemisection of the auditory nerve, avoiding loss of hearing, in Ménière's disease. In none of the three cases in which the vestibular branch was operated on has there been a single subsequent attack of dizziness for thirteen, seven and four months, respectively, although transient dizziness on turning the head occurs in most cases after section of the nerve. Hearing is usually badly damaged by the time the patient comes to operation. It may be that early operation would save the hearing, but this is not certain, as the cause of Ménière's disease is not known. A statistical analysis of the symptoms in forty-two cases is given; in thirty-nine the eighth nerve was divided and in three the vestibular branch was divided.

The essential features of Ménière's disease are recurring dizzy attacks, unilateral partial deafness and tinnitus in the affected ear. Attacks due to cerebral arteriosclerosis and other known and unknown causes are bilateral. Tumors in the cerebellopontile angle rarely cause comparable attacks of dizziness. If dizziness occurs it is usually only on changing posture and is of brief duration and does not assume the importance of well defined attacks. Deafness and tinnitus may be due to aneurysm of the basilar artery, but the dizziness is not similar to that seen in Ménière's disease. The same is true of so-called acoustic tumors. The differential diagnosis, therefore, between Ménière's disease and tumors in the cerebellopontile angle can be made, with rare exceptions (such as in the one case of a basilar aneurysm reported), solely on the basis of the subjective symptoms. In cases of pseudo-Ménière disease, the spells of dizziness are the same as in cases of Ménière's disease, but tinnitus and deafness are absent. Dandy suggests that some of the cases of pseudo-Ménière' disease may be cases of Ménière's disease in the early stage. In five cases there was bilateral deafness, making it difficult to choose the side on which to operate. It cannot be definitely said that Ménière's disease is ever bilateral.

The author has performed the operation forty-two times since Jan. 11, 1927, and in not a single instance has there been an attack of dizziness subsequent

to the operation. Coleman and Lyerly reported eleven cases in which operation had been performed, and Cairns and Brain reported four cases with identical results. Evacuation of the cisterna magna before elevation of the cerebellar hemisphere is important, giving ample room and making it possible to avoid severe injury to the cerebellum. The operation is done under local anesthesia without pain, but Dandy much prefers the use of avertin because there is no swelling of the brain, with consequent reduction of room in which to work, and postoperative pneumonia occurs less frequently. Local anesthesia is preferred to the use of ether. The facial nerve was severed in two of the earlier cases. In three cases, Bell's palsy appeared after the operation but cleared up completely. In four cases diplopia followed the operation, but it cleared up in a few days; three of these patients had had diplopia during an attack. Nystagmus and vertigo following the operation were transient, disappearing usually within a week or ten days. Dandy differentiates between vertigo, dizziness and disturbance of balance on moving the head. In one patient dizziness on turning the head persisted for three years. Acoustic tumors and other tumors necessitating division of the eighth nerve were not followed by transient dizziness. Therefore, Dandy believes that the dizziness is due to the underlying pathologic changes of Ménière's disease and that the lesion must be in the central pathways responsible for dizziness. Tinnitus disappeared after operation in twenty cases, remained unchanged in seventeen and was diminished in two. It was never increased. A patient with tinnitus and total deafness without dizziness continued to have the tinnitus after division of the eighth nerve. Therefore, one can never promise that division of the nerve will cure the tinnitus, but the chances are 50 per cent that it will disappear, with an additional 20 per cent that it will be improved.

Dandy has not been able to find a single report of necropsy in a case of Ménière's disease. Unlike tic douloureux, in which changes in the sensory root are present, no gross changes in the nerve were observed in any of the forty-two cases, but Dandy believes that the attacks are due to a lesion in the auditory nerve and not in the semicircular canal, although he also speculates on the possibility that the lesion may be diffuse.

The vestibular branch of the auditory nerve is located anteriorly in the nerve bundles. In only two cases were the cochlear and vestibular branches separate. Therefore, Dandy assumed that division of the anterior half would include all the vestibular fibers, but in order to be safe an additional incision into the cochlear half was made, and no loss of hearing resulted. He has not seen any cases with total deafness in which cure was obtained. He proposes early operation and says that there is hope that bilateral section of the vestibular nerve may be performed successfully in attacks of pseudo-Ménière disease. In the cases in which Dandy operated, in which the attacks ceased, hearing was unimpaired. This may be simply a long interval between attacks. It is hoped, but is not yet assured, that cure of the disease in the early stages may prevent the progressive loss of hearing that is inevitable if the condition is left untreated.

HUNTER, Philadelphia.

THREE CASES OF ARACHNOIDITIS OF THE POSTERIOR FOSSA. P. WINTER, F. RAPPOPORT and H. BERDET, Rev. d'oto-neuro-opht. **11**:651 (Nov.) 1933.

Many cases of tumor of the posterior fossa, particularly of the acoustic nerve, are accompanied by arachnoidal reactions which cause adhesions, fibrous bands and cysts. Since the work of Cushing, Horrax, Bailey and Frasier, it is well known that there are a number of cases of arachnoiditis in which careful examination, both macroscopic at the time of operation and microscopic following autopsy, reveals no evidence of tumor. These cases fall into two groups: (1) those presenting mental disorders, crises of epilepsy, motor difficulties, with or without papilledema, and dilated ventricles (arachnoiditis of the cisterna magna); (2) those exhibiting staggering, lateropulsion, nystagmus, vertigo and neuralgia of the fifth nerve. Three cases belonging to the second group are reported. In the first, there was unilateral involvement of the fifth, sixth, seventh and eighth nerves,

associated with a vestibular syndrome which resembled closely that of tumor of the acoustic nerve. The illness began, seven years before the observation was made, with tinnitis in the right ear but without appreciable diminution of hearing. Vestibular reactions on the right side were completely abolished. Clinical signs of hypertension were absent even after several years, and this, taken in connection with disturbances of several other cranial nerves and with lack of deformity of the ventricles, points more to arachnoiditis than to tumor. None of these signs has an absolute value in eliminating the diagnosis of tumor of the angle, and only the findings at operation can be decisive. The presence of a tumor situated higher up in the posterior fossa is not probable in view of the abrupt appearance of signs of cerebellar involvement, facial paralysis and difficulties in hearing; in cases of tumor the symptoms develop more gradually and are progressive.

In the second case the syndrome referable to the eighth nerve resembled closely that of tumor; deafness preceded the appearance of other symptoms for several years; it was complete and was accompanied by abolition of the vestibular reflex. The history and course of the disease, however, and the ocular signs furnished important evidence in favor of a diagnosis of arachnoiditis. Clinical signs of hypertension were transient; the headache was not marked, and the slight lowering of visual acuity did not change. No papilledema existed, but slight pallor of the temporal segments of both papillae and lateral homonymous hemianopia in the left superior quadrant were present. These discordant symptoms could be explained only by diffuse multiple lesions.

The third patient had an attack of grip eleven years before observation, during which deafness and tinnitus appeared suddenly in the left ear and were soon followed by vertigo and disturbed equilibrium. A diagnosis of tumor was eliminated by reason of the mild character of the headache and the absence of occipital pains, cerebellar disturbances and changes in the eyegrounds after several years of evolution. The elective and isolated involvement of the acoustic nerve is incompatible with the hypothesis of tumor of the region developing over such a long period. The sudden appearance of deafness, tinnitus and vertigo during an attack of grip is in favor of a diagnosis of neuritis of the eighth nerve, but it is not usual for both the cochlear and the vestibular division to be simultaneously involved in such a definite fashion.

All three patients were operated on by the occipital route, and the diagnosis was confirmed. In the diagnosis of arachnoiditis the negative signs (lack of intracranial hypertension and of ventricular distention) are important. The variety of symptoms is characteristic of arachnoiditis. It may simulate tumor of the acoustic nerve, a temporal lesion or a lesion of the vestibular apparatus. The operative findings were the same in all three cases: abundance of cerebrospinal fluid, cystic appearance of the arachnoid and a feltlike arachnoid enveloping the nerves of the region. It is advisable to choose a quiescent period of the disease for surgical intervention and, when tumor can be eliminated with reasonable probability, to precede the operation on the posterior fossa by a subtemporal decompression, followed by appropriate medical treatment. Section of the eighth nerve is indicated in cases attended by deafness and severe vertigo, but this operation is not always followed by disappearance of the tinnitus.

DENNIS, San Diego, Calif.

INFLUENCE OF FIXATION ON THE VISUAL ACUITY. F. H. ADLER and MAURICE FLIEGELMAN, Arch. Ophth. **12**:475 (Oct.) 1934.

In ordinary use the eyes are never entirely at rest but are constantly moving. The visual axes are continually changing so that images of objects in the outside world are brought to lie on the macular region of each eye. In order to discriminate the finer details of an object it has often been assumed that the image of an object must rest on the fovea, permitting the parts of the image to stimulate a definite pattern of cones. The term fixation is used in this connection to signify that under these conditions the eye remains still. This conception of fixation has been strengthened by the close correspondence of the size of the cones in the fovea

and the threshold for the acuity of vision as measured by the minimum separable. Further, no thresholds have been reported for the minimum separable lower than the angular distance corresponding to the diameter of a foveal cone. It was on this basis that test letters were first constructed for determining visual acuity. Since then considerable experimental work has been presented to show that there is no fundamental physiologic basis for the use of the 1 minute angle in the construction of these letters, however useful it may be from a practical point of view.

The experimental work of Adler and Fliegelman was designed to reinvestigate the following problems: 1. How accurate is fixation when a constant pattern such as a cross-hair on a white background is looked at? 2. How accurate is fixation when a displacement in a part of a line is being examined? As a result of their findings, the authors decide that fixation is only a relative term. Even during the most exact fixation of the visual axes the eyes are in continual motion, so that a point image must traverse at least from two to four cones in the fovea. Even this degree of fixation does not last more than two-tenths second, for owing to constant tonic impulses to the extra-ocular or cervical muscles, the eyes or the whole head shows slight rhythmic deviations which must carry a point image over from ten to fifteen cones in a second. Added to this are large movements of which the subject is conscious when he is making a strenuous effort at steadiness and which he cannot prevent, which carry the image over at least twenty-five cones.

One can say with confidence that fixation is certainly limited to the true fovea centralis. The conception of the thresholds of visual acuity must be based on some theory which treats of the fovea acting as a whole and not on the discrete stimulation of individual cones or fractions of cones, as has sometimes been attempted.

According to the conception of motion of the visual axes just given, it is proper to interpret the authors' findings in another way. If the normal person must have the image in constant motion on the fovea, where the cones are closely packed together and therefore numerous, it is all the more necessary to increase this motion when the fovea is defective, so that the image will sweep over a similar number of cones in regions where the cones are more sparsely scattered. Hence, patients with congenitally defective foveas show these rapid searching movements for the purpose of having a large number of cones stimulated. If the fovea becomes defective in later life, however, this corrective mechanism cannot be employed because the patient has already formed the habit of keeping the eyes firmly fixed so that the image will fall on the fovea. For this reason the searching movements are not seen in patients with macular disease acquired later than infancy.

SPAETH, Philadelphia.

THE RELATION OF MENSTRUATION TO PERSONALITY DISORDERS. EDWARD A. ALLEN and GEORGE W. HENRY, Am. J. Psychiat. **13**:239 (Sept.) 1933.

Allen and Henry have studied the correlation between menstrual and personality disorders in 100 cases: 34 cases of schizophrenia, 35 cases of manic-depressive psychosis, 13 cases of neuroses and 18 cases classified in a miscellaneous group. The ages of the patients ranged from 14 to 47 years. During the manic phases, the patients with manic-depressive psychoses showed no significant interruption of the menstrual cycle. Varying periods of amenorrhea, however, were observed during depressive episodes; generally, the deeper the depression the more protracted the amenorrhea. In almost all of these patients sexual development was anatomically normal. Among the schizophrenic patients, menstrual disorders were common in those with the catatonic type and rare in those with the simplex type. Patients in a chronic stage of dementia praecox generally menstruated without interruption, while those in the acute stages of this psychosis showed irregularities, which were more pronounced during periods of active hallucinosis or catatonic stupor. Gynecological examination in these cases revealed evidence of sexual underdevelopment, primary or secondary, in nearly 50 per cent of the schizophrenic patients. Prepsychotic menstrual disorders were also far more frequent in this group than in any other. Among the psychoneurotic patients, more or less prolonged periods of amenorrhea occurred in about half the cases. This interruption of the cycle

was commonly associated with painful emotional responses. In the miscellaneous group, menstrual irregularities occurred chiefly among those with schizoid, toxic or alcoholic tendencies.

In an effort to stimulate the menstrual flow, Allen and Henry employed glandular therapy without success. They used thyroid, preparations of the ovary, corpus luteum and pituitary, estrogenic substances and the gonad-stimulating principle from the urine of pregnant women. In some instances, notably in cases of involution melancholia, some subjective improvement was observed; but neither the period of the amenorrhea nor that of the depression was reduced by glandular treatment. The authors, in fact, express doubt as to the wisdom of attempting to force a physically depleted or sexually immature woman to bleed from her uterus.

Henry and Allen discuss the psychology of personality fluctuations in normal women during the menstrual period. Among psychotic patients, the personality responses are distorted or intensified; the difference is one of degree, however, rather than of quality. The schizophrenic patient rationalizes any inadequacies with more or less systematized delusions or overcompensates with erotic, exhibitionistic behavior. The latter is also observed in hypomanic women. Other manic patients show irritation at the limitations imposed on their activities or demonstrate wish fulfilment fantasies in reference to fear or hope of pregnancy. Among the depressed, the sense of unworthiness is aggravated.

In her discussion of this paper, Dr. McCall criticized the lack of a control group of normal women with similar menstrual irregularities. In answer, Dr. Henry pointed out that a careful charting of the emotional fluctuations of the normal woman would be necessary before any such control group could be utilized. The authors stress the need of the careful study of the menstrual life of both psychotic and normal women in surveys of psychologic interest.

DAVIDSON, Newark, N. J.

FACIAL PARALYSIS AND LABYRINTHITIS: ANATOMIC EXAMINATION OF THE FACIAL NERVE. ANDRÉ-THOMAS and L. GIRARD, Rev. d'oto-neuro-opht. **11**:664 (Nov.) 1933.

A patient entered the hospital on Dec. 5, 1932, with facial paralysis of peripheral type on the right side and pain in the teeth and ear. In 1921, 1922 and 1929 the patient underwent several operations for osteomyelitis of the humerus. Three months before her admission to the hospital a vertiginous attack, with diminished hearing in the right ear, had occurred. Examination revealed a normal drum membrane, total deafness of the right ear, a few nystagmus twitches and almost total paralysis of the right facial nerve; no Romberg sign or spontaneous deviation was present. There were no signs of cerebellar disease. Lumbar puncture on December 8 revealed 696 polymorphonuclears per cubic millimeter. On December 9 the ear began to discharge, and a positive Kernig sign and stiffness of the neck were observed; the spinal fluid contained 845 cells per cubic millimeter. Operation revealed a normal mastoid process, but the tympanum was filled with pus which came from a large extradural abscess by way of a fistula through the oval window. The labyrinth was opened. Drainage was inadequate, and the patient died in coma six days later. At autopsy the fistula was found to open on the endocranial surface slightly external to the fallopian hiatus, having passed above the elbow of the fallopian aqueduct and the seat of the geniculate ganglion. Serial sections of the facial nerve, including the geniculate ganglion and extending to the endocranial portion, showed the following changes: the connective tissue sheath was thickened and contained masses of nuclei; these masses were sparse in the geniculate ganglion; the pericapsular cells were not proliferated; the masses were composed of fibroblasts, plasmocytes and mononuclear and polymorphonuclear cells. The masses were numerous at the level of the passage of the petrous nerves into the facial nerve. The lesions situated in the portion of the nerve inside the ganglion and in the internal auditory meatus were the most intense. Foci of hemorrhage in the sheath and in the nerve itself, separating the fibers by pools of blood, were present. The nerve fibers were poorly stained, and the axis-cylinders were swollen, irregular

and disaggregated. The neighboring arachnoid showed considerable proliferation of nuclei but relatively few polymorphonuclear cells. The assumption is that a benign otitis complicated by labyrinthitis occurred in September and that the process remained latent until the facial paralysis occurred. The hypothesis is suggested that staphylococci from the site of the osteomyelitis might have hibernated in the labyrinthine capsule, where they remained until awakened to activity by some favorable circumstance. It is known that staphylococci have the ability to live a long time in osteomyelitic foci and to emigrate and that they have a predilection for osseous tissues when their primary seat has been in bone.

DENNIS, San Diego, Calif.

THE ETIOLOGY OF HEADACHE: I. HEADACHE PRODUCED BY THE INJECTION OF AIR FOR ENCEPHALOGRAPHY. CHARLES A. ELSBERG and ROBERT W. SOUTHERLAND, Bull. Neurol. Inst. New York **3**: 519 (March) 1934.

Elsberg and Southerland question the widely accepted belief that headache is produced by stretching or by other changes in the dura and the pia mater. They state that during cranial operations under local anesthesia traction and pressure on these membranes do not produce headache or pain. Various theories of the causation and mechanism of headaches are reviewed, and the opinion is held that variation in the intraventricular pressure is an important factor in the production of headache. The influence of variation in intraventricular pressure in stimulation of the thalamus, which forms part of the walls of the lateral and third ventricles, is considered a probable factor in producing disturbances in the function of the thalamus, which in turn result in an excessive response to effective stimuli.

Eighty-six patients on whom encephalographic studies were carried out were carefully observed for the relationship of the severity and the location of headache to the position of the head, the amount and the location of the injected air and a shift in the location of headache with a change of posture and of location of air in the ventricles. In fifty-one cases roentgenograms were taken at intervals of one or two days until all air had disappeared in an attempt to determine the relationship between the headache and the amount and location of air remaining in the cranial cavity. Headache of varying degree occurred in all subjects.

Headache was produced quickly after the injection of a small amount of air in patients whose ventricles were normal in size or who had an expanding lesion in the cranial cavity. More air was necessary to produce headaches when the ventricles were dilated. Roentgenograms taken at the time the patient first complained of headache showed air in the lateral or third ventricle in 93 per cent of cases. In twenty of the eighty-six cases air was found underneath the tentorium immediately after complaint of headache, but in all these air was also present in the third and lateral ventricles. In only eight cases was air seen over the surface of the brain at this time. Headache had usually disappeared before the air was entirely absorbed, and the severity and the duration of the headache did not seem proportional to the amount of air remaining in the ventricular system. The authors conclude that these findings indicate that the presence of air in the subarachnoid space over the cortex is not responsible for the headache which occurs during encephalography, whereas the relationship between headache and air in the lateral and third ventricles is of decided significance.

KUBITSCHEK, St. Louis.

SWELLING OF THE NERVE HEADS WITH ARACHNOIDITIS AND UNUSUAL CHANGES IN THE VISUAL FIELDS. EDMUND B. SPAETH, Arch. Ophth. **12**:167 (Aug.) 1934.

Spaeth reports a case of migraine that had been present for many years, associated with progressive swelling of the nerve heads, edema, hemorrhages and progressive contraction of the nasal fields, even to their complete loss. This was

especially evident when small test objects were used. A diagnosis was made of possible neoplasm of the optic nerve at the chiasm.

At operation the vessels were adherent, with localized arachnoiditis and with an aneurysm-like swelling of the right anterior cerebral, the right middle cerebral and the right internal carotid artery. The vessels were adherent to the meninges and to the chiasm. General medical examination gave negative results, and there were no signs of localized or generalized arteriosclerosis. The patient made an uneventful recovery after surgical relief of the arachnoid adhesions.

The conclusions are: Any case of binasal hemianopia should be carefully investigated before it can be considered a genuine case of this rare defect. Visual fields no more typical of pure damage to the nerve fiber bundles than those presented in this case have been reported as representing binasal hemianopia. The case reported presents unusual fields, which under conditions of greatest damage simulate binasal hemianopia and may progress to such a degree of binasal field loss that later in the course of the condition true differentiation will be impossible. It is likely that certain fields reported as being examples of binasal hemianopia should and will fall into this class. Although in the case presented the greatest loss lay in the nasal halves of the field, it is not one of true hemianopia.

Angioscotomas and defects in the nerve bundles are probably independent, and certainly are early, in any given case. It appears that changes in the visual field attributable to pathologic variations of the angioscotomas are later modified by associated defects in the nerve bundles and also that this can arise in cases of intracranial vascular disease with arachnoiditis through modification of the circulatory or vascular supply of the brain and the retina.

The Seidel sign and the Bjerrum scotoma, so often considered as the onset of defects in the nerve bundles, may be in many instances angioscotomas of pathologic size, as they seem to have been in this case. Further, they are not of necessity diagnostic of glaucoma. Considering the field defects found in this case with known vascular pathologic changes and comparing them with the defects found so frequently in cases of glaucoma, one is impressed by the great rôle that the retinal circulation (both blood and lymph) must play in the symptomatology of glaucoma.

SPAETH, Philadelphia.

CASTRATION IN FORTY SEXUALLY ABNORMAL PERSONS. A. W. HACKFIELD, Monatschr. f. Psychiat. u. Neurol. **87**:1 (Oct.) 1933.

The results of operative removal of the gonads in forty sexually abnormal persons are reported. Most of the patients were observed for many years. The operation was performed only on persons who had repeatedly committed crimes of a sexual nature and for whom correctional and medical treatment, including psychotherapy and institutional care, had been totally unsuccessful. A group of twenty-five male psychopathic patients, most of whom were exhibitionists, abandoned their perverse practices and were able to engage in normal activities as useful members of society. In contrast to this, no improvement whatever was observed in a group of six female patients who were extremely promiscuous sexually or who exhibited states of excitement during menstruation. A group of nine male and female psychotic patients presenting abnormal sexual practices failed to show improvement with respect to the psychosis, and only one ceased the perverse activities. Physically, no unfavorable results were noted. In fifteen cases a moderate increase of weight occurred, and eleven of the twenty-five psychopathic male patients showed loss of facial or body hair. Interestingly, eleven members of this group and four of the six psychotic male patients retained their ability to perform the sexual act. These observations indicate that the seat of the libido cannot be exclusively in the gonads. It is known that some libido is fixed in the thyroid, pineal and pituitary glands and that cerebral components play an important part in erections and in the sexual act. It is thus possible that reserves exist and that other systems can to a certain extent take over the function of the gonads. This view receives support from the fact that men who were active

heterosexually prior to castration retained their potency better than the others. The therapeutic effect of castration in males is explained by the assumption that the physiologic sex tension which is not able to obtain a normal outlet in these abnormal persons finally overcomes the rather weak inhibitions that they possess, leading thereby to perverse acts. While remnants of libido may remain after castration, the tension is distinctly decreased and is no longer able to overcome the barriers of morality. The lack of improvement in the female patients is due to the fact that the passive rôle of women in the sexual act allows erotic excesses after operation if the general mental attitude is not altered. Hackfield concludes that in carefully selected cases castration is a successful method of treatment for sexual perversions.

ROTHSCHILD, Foxborough, Mass.

THE PHYSIOLOGY OF ELECTROPYREXIA. CLARENCE A. NEYMANN and S. L. OSBORNE, Am. J. Syph. & Neurol. **18**:28 (Jan.) 1934.

Machines for producing fever depend on the application of either external heat (such as electric blankets and cabinets) or of penetrating heat (high frequency types). Electric blankets produce slowly rising temperatures, and when employed should be used with care so that the temperature of the surrounding atmosphere remains below 130 F., unless the air is kept in constant motion. Temperatures in excess of 120 F. produced by electric blankets are dangerous and futile, for they do not perceptibly quicken the rate of rise of body temperature. Fever of this type, furthermore, is more exhausting than fever produced with diathermic or radiothermic apparatus. During this type of treatment (external application of heat) perspiration is less profuse than when penetrating heat is used. In either case the basal metabolic rate rises during the treatment an average of 7 per cent for each degree of elevation of temperature. Body liquids will concentrate, so that the blood cells, hemoglobin, nonprotein nitrogen and urea constituents of the blood will rise. Injections of scopolamine hydrochloride during fever therapy will inhibit sweating and cause the axillary temperature to rise above the rectal temperature. Neymann and Osborne believe that the use of antihydrotics is contraindicated.

In order to ascertain the exact temperature of parts of the body during treatment, the authors soldered thermocouples into needles. During penetrating heat they found that the temperature of the lumbar portion of the spine rose rapidly to 106 F. The rectal temperature lagged behind for a while but finally exceeded that of the lumbar portion of the spine, eventually reaching 108 F. The temperature of the cisterna magna—probably closely approximating that of the brain itself—reached 107.5 F. at the height of the treatment. Exposed or even slightly exposed surfaces cooled rapidly. The superficial and subcutaneous tissues did not reach these high temperatures or did not remain sufficiently warm for any length of time—a fact which probably accounts for the present failure of fever therapy in cases of early syphilis. In order to cure primary syphilis it is necessary to maintain a temperature of 107.5 F. (42 C.) for an hour or of 106.5 F. (41 C.) for two hours. This temperature should be sustained throughout the body. In robust patients it is possible to carry this out with the central nervous system, the liver and the rectum, but the surface of the body and the superficial and subcutaneous tissues cannot be maintained at this temperature.

DAVIDSON, Newark, N. J.

DEMONSTRATION OF VEGETATIVE DISTURBANCES BY MEANS OF HYPERVENTILATION AND THE PHYSICOCHEMICAL BASIS UNDERLYING THEM. A. BINGEL, Deutsche Ztschr. f. Nervenh. **132**:123 (Sept.) 1933.

In many functional diseases of the nervous system the symptomatology suggests a disturbance of the vegetative nervous system. To demonstrate the susceptibility objectively as well as the basis underlying abnormal reactions of the vegetative nervous system, Bingel hyperventilated patients with such disturbances, using other patients as controls. Hyperventilation as a method for studying vegetative phe-

nomena was suggested by Pette in 1930 following the observation that it produces in some persons a symptom complex allied to that of disturbances of the vegetative nervous system. This method of artificially producing a definite symptom complex Bingel suggests as an aid in diagnosing obscure or suspected cases of disturbances of the vegetative nervous system. In addition to observing the effects of hyperventilation, Bingel also studied the changes in metabolism, including that of the calcium, inorganic phosphates and potassium, and the changes in the electric response and chronaxia. Hyperventilation was maintained on an average for thirty minutes. Careful attention was given to the depth of respiration, especially to the expiration. When tetanic manifestations appeared early, respiration was resumed more quickly. Bingel found that with few exceptions in patients with involvement of the endocrine system and the vegetative nervous system, hyperventilation will produce tetany within from three to twenty minutes, a susceptibility which is not found in controls. In a few of the latter mild symptoms may appear after prolonged hyperventilation. In each case the time element is taken as an indicator of the patient's reaction. The relatively quick reaction of vegetatively disturbed patients to hyperventilation indicates an increased susceptibility of the entire vegetative system to the humoral changes brought about by hyperventilation. The humoral changes are demonstrable by an increase in the chronaxia of the musculature and by a lowering of the rheobase, by the metabolic shifting toward the alkaline side and by a frequent decrease in the ultrafiltrable serum calcium. Bingel's finding confirms György's conception that the diminution of ionized calcium in the serum is responsible for the tetanic symptoms observed after hyperventilation. A change was also observed in the total calcium content and in the inorganic phosphates. Bingel affirms that hyperventilation offers an aid in diagnosing disturbances of the vegetative nervous system.

BERNIS, Rochester, N. Y.

OBJECTIVE TINNITUS AURIUM. SAMUEL IGLAUER, Arch. Otolaryng. **18**:145 (Aug.) 1933.

In rare instances tinnitus may be objective owing to the spasmodic rhythmic contraction of muscles related to the eustachian tube in cases of rhythmic contraction of the palatal muscles or the tensor tympani muscle, or due to sounds of vascular origin. Cases illustrating the latter are reported by Iglauer in which auscultation over or near the great vessels on the affected side revealed a sound. In several cases the tinnitus was lessened when the patient turned toward the affected side. It was greatest when the head was to the front and was less evident when the head was turned to the opposite side. The bruit was synchronous with the pulse. Four cases are reported.

After a review of a meager literature on the results of rotation of the head on intracranial pressure Iglauer quotes experiments on pressure on the external jugular veins in ten cases. The maximum pressure was higher when the subject was upright than when he was recumbent. In each case the minimum pressure was present when the head was on center. The maximum pressure was observed when the head was rotated toward the side being tested; the next highest pressure, when the head was rotated toward the opposite side.

Iglauer thinks that the well known difference in the size of the lateral sinuses may result in a slight whirlpool, which would create a sound. Several autopsy reports from the literature are offered in support of this assumption. The relation of congenital aneurysmal angiomas, vascular tumors, meningiomas and gliomas and the suggestion of Jacobson that "subjective and objective sounds may be transmitted headward in the direction of the blood current from their origin in atheromatous and possibly dilated carotid arteries" are mentioned. The author also mentions ligation of the carotid artery as a possible cure, but he cites cases in which this was of no avail. He advocates ligation of the jugular vein. Iglauer has apparently overlooked the article by E. P. Fowler in which it is mentioned that constriction of the veins of the neck by a collar or tight band lessens tinnitus.

HUNTER, Philadelphia.

MIGRAINE AND THE HYPOPHYSIS. P. L. DROUET, L. MATHIEU and L. COLLESSON, Rev. franç. d'endocrinol. **12**:137 (April) 1934.

The authors have investigated the presence of principles of the posterior lobe of the pituitary gland in the urine of patients suffering with migraine. The technic consists of the injection into the dorsal lymph sac of a frog of a small amount of nocturnal urine taken from patients with migraine. In positive reactions, the color of the skin turns black. This reaction is supposed to be caused by the "melanophorotropic" element, which originates in the posterior lobe of the pituitary gland and is present in persons suffering from migraine. Altogether fifteen patients (nine women and six men) were studied. Three hundred and twelve specimens of urine were injected into six hundred and twenty-four frogs. The presence of this hypophyseal principle in the urine of patients with migraine was established in thirteen of the fifteen cases. The authors believe that there is no absolute synchronism between the duration of a positive reaction and the migrainous attack. There were variations in the same person as well as in the whole group of cases. Sometimes the phase of the positive reaction preceded the attack of migraine, was present during the attack and persisted for a few days after cessation of the attack. At other times the chronological relationship was similar to the preceding example, but with the exception of a negative reaction for one day at a time when the migrainous attack was at its height. Occasionally the melanophoric reaction preceded the attack and continued during the attack, but became negative as soon as the attack ceased. At other times the reaction was noted to be positive only after the attack of migraine had already developed and continued to remain positive for a few days after its cessation. Although there is a close parallelism between the migrainous attacks and the phases during which the principle of the posterior lobe of the pituitary gland is present in urine, there is, however, no absolute synchronism in a mathematical sense. NOTKIN, Poughkeepsie, N. Y.

THE HISTOPATHOLOGY OF HUMAN CHOROID PLEXUS AND EPENDYMA. G. BIONDI, Arch. f. Psychiat. **101**:666 (Feb.) 1934.

This report was made on the basis of a study of ninety-three cases, in twenty-five of which there were no signs of mental or of nervous diseases. Histologic examinations were made on sections stained primarily with the special silver stain devised by the author. In addition, the Romeis sudan stain and the Holzer, the Achucarro and other methods of staining were employed. The following are the results of the study: In persons over 60 years of age, regardless of the presence or absence of any mental or nervous disease, the epithelial cells of the plexus show special "silver structures." These consist of more or less clearly demonstrable rings which take the silver stain and develop around a central lipoid nucleus. In some cases they can be found more or less definitely developed in persons between 40 and 60, but they are never found in persons less than 40 years of age. In persons over 60 there is also found diffuse connective tissue sclerosis in the stroma of the plexus. This, however, may also be present in younger persons, occurring sometimes as early as the third decade. Similar silver structures occur in older persons in the epithelium of the ependyma of the ventricles. These, too, are absent in persons below the age of 40. In persons of all ages, regardless of the two conditions described, various forms of pathologic pictures were found in the plexus. These consisted of circumscribed scleroses, reduction of the parenchyma, cysts, concrements, fatty degenerations, etc. No parallelism was found to exist between any single type of plexus or ependymal pathologic process and certain types of psychoses or diseases of the brain. Biondi comes to the conclusion that the only specific plexus and ependymal changes are those that occur in old age. These, however, need not in any way be related to special diseases. As a fact, some of the most pronounced changes were found in cases in which there were no clinical signs of senile degeneration. MALAMUD, Iowa City.

PSYCHO-ANALYTIC TREATMENT. EDITORIAL COMMENT, Brit. M. J. **2**:1175 (Dec. 23) 1933.

This article is an editorial comment on an article by the late Dr. Leo Kessel and Dr. H. T. Hyman which appeared in *The Journal of the American Medical Association* (**101**:1612 [Nov. 18] 1933). Of the thirty-three cases studied, results were classified as bad in sixteen; seven of the patients in this group were psychotic. The results in four cases were classified as good, with qualifications; in this group the patients became symptom-free, but the authors considered that the results might be attributed to sexual satisfaction as much as to the analysis. Since this sexual satisfaction was experienced outside marriage, the beneficial nature of the cure from the standpoint of society may be questioned. Improvement of marital relations is a more frequent outcome of analysis than is divorce. In thirteen cases the results are classified as satisfactory. Cures were obtained in five of these, and in the opinion of the authors this could not have been brought about by any other method. Five patients showed improvement, though cure was not complete, and in three instances of behavior problems the analyst succeeded in producing the desired result without conclusion of a formal analysis. It is interesting to note that the five cured patients were all of the intellectual class and under 30 years of age.

The editorial comments that although statistically the results reviewed in the paper are not impressive it is probable that they would compare favorably with results with any other technic, for treatment of functional mental disorders was not conspicuously successful before the advent of freudian methods. The present tendency among psychoanalysts is to establish a method, but whether the methodologic approach in the treatment of mental diseases is ever likely to be successful remains for the future to decide, for in mental illness, more even than in physical illness, it is the patient who must be treated and not the disease.

FERGUSON, Niagara Falls, N. Y.

EXPERIMENTAL RESEARCHES ON THE SEAT OF ACTION OF PHENOBARBITAL IN THE BRAINS OF RABBITS. ERNST SAHLGERN, Acta psychiat. et neurol. **9**:129, 1934.

Researches of Maunthner, Economo and Hess pointed to the existence of a sleep-regulating center in the floor of the third ventricle. Keeser and Keeser demonstrated an accumulation of phenobarbital in the region of the diencephalon and thalamus in animals submitted to chronic intoxication with this drug. Sahlgern undertook experiments on rabbits to obtain further evidence on the seat of action of phenobarbital in the brain. Trephination was first carried out, and after from one to two days 1 cc. of solution of phenobarbital sodium to which china ink was added was injected into various regions of the brain. The sleep reaction was observed and recorded for a period of several hours after the injection. The animals were killed, and the distribution of china ink was studied in serial sections of the brain. In all the animals into which the injection was made in the infundibular region a state of sleep developed within about five minutes and lasted from one-half to two hours. Sections of the brain revealed the presence of china ink around the infundibulum. All animals into which the injection was made in the region of the brain other than the infundibulum showed no, or only a delayed, sleep reaction. In order to control the experiments, Sahlgern injected methyl acetamide (a solvent of phenobarbital) into one series of animals and a solution of sodium chloride into another series. The injection did not induce a sleep reaction in any of the animals, although the presence of china ink permitted the localization of the seat of injection in the infundibular region. The author concludes that phenobarbital, in producing sleep, acts on the infundibular region and thus that this region plays an important rôle in the regulation of sleep.

YAKOVLEV, Palmer, Mass.

OPTOCHIASMAL ARACHNOIDITIS. P. PUECH, M. DAVID and M. BRUN, Rev. d'oto-neuro-opht. **11**:641 (Nov.) 1933.

In general, the diagnosis of optochiasmal arachnoiditis is possible before operation. It is differentiated from tumor by the history of a previous infectious process,

often in the cavities of the head, and by the abrupt onset of failing vision that rapidly progresses to blindness. In the beginning, the eyegrounds are frequently not changed (retrobulbar neuritis); optic atrophy of the primary type quickly follows; still more characteristic is the early appearance of papilledema and pallor of the nerve head; papillary changes which, even in cases in which edema is present, are almost always preceded by serious impairment of visual acuity. Irregular narrowing of the visual fields without clearly systematized characteristics occurs; even when the hemianopia is temporal, the retraction is irregular and atypical; central scotomas are frequent and appear early. There are no roentgenographic signs of tumor, and ventriculography shows symmetrical ventricles with absence of deformity imputable to tumor. In cases of tumor the evolution is slower and is progressive, the beginning of ocular difficulties is insidious and for a long time temporal hemianopia is clearcut while central vision is preserved.

Surgical intervention after the technic of Vincent is ordinarily simple and productive of no ill effects. In May 1932 Vincent reported death in three of seventeen cases following operation. Since then operation has been performed in ten cases without a death. Results show that when the blindness has existed only a short time recuperation after operation may be expected.

Two cases are reported in detail. The report is accompanied by charts of the visual fields and drawings showing adhesions that compressed the optic nerve.

DENNIS, San Diego, Calif.

THE MIGRAINOUS PATIENT. GRACE TOURAINE and GEORGE DRAPER, J. Nerv. & Ment. Dis. **80**:1 (July); 183 (Aug.) 1934.

Fifty patients with migraine, thirty-seven women and thirteen men, have been studied by the authors for personality and constitutional peculiarities. There was prominence of the maxillae, supra-orbital ridges and glabella, and a characteristic formation of the skull tending toward acromegaly was found in persons with a long face. The intelligence of the patients was outstanding, but emotional development appeared to be retarded. The patients seemed to withdraw from reality rather readily and were of the introvert type. The headache is individually characteristic, occurring in the same pattern and under similar circumstances. Situations involving the loss of home protection, the necessity to stand alone and to grow up and the advent of personal adult responsibility mark the moments in life when the headaches first appear. Unconsciously, the migrainous woman is unable to view herself as an individual apart from her mother, and the idea of separation is apparently insupportable. Men take a more passive attitude toward the mother and continue to live within her protection. Not one of the thirty-seven women seems to have made a successful adult heterosexual adaptation.

Familial predisposition to migrainous headache is evident, and the character of the attack is often similar in several afflicted members of a family group. In most cases inheritance is through the maternal line. Unwitting imitation of the migrainous ancestor appears to be an important aspect of the genetic interpretation. The attack is a syndrome comparable to any other neurosis developing in a special constitutional type. The physiologic processes producing the headache are secondary to and precipitated by emotional conflicts.

HART, Greenwich, Conn.

VISUAL FIELD DEFECTS IN PREGNANCY. C. E. FINLAY, Arch. Ophth. **12**:207 (Aug.) 1934.

In 1922, Finlay read a paper entitled "Bitemporal Contraction of the Visual Field in Pregnancy." Subsequently, several investigators have published both confirmatory and nonconfirmatory findings. In view of some nonconfirmations, Finlay again studied the subject in 108 consecutive cases. As a result of these investigations he believes that defects of the visual field occur in the majority of cases of normal pregnancy. These are of the nature of bitemporal contraction, with some tendency to limitation to a quadrant or intensification in a quadrant.

With colors, there was some tendency to concentric contraction, which was especially noticeable in tests with small objects. The findings were more apparent in the last months of pregnancy and were most marked after successive pregnancies. Age did not seem to have any influence on the production of the defects. A greater predisposition to such defects seems to exist in the colored race and in Latin races.

Finlay believes that the cause of contraction is a mechanical compression of the normally hypertrophied hypophysis and that even when it does not directly compress the chiasm it may produce vascular changes of the nature of arterial or venous engorgement or anemia in or around the chiasm. These may be accompanied by more or less secondary edema, with secondary changes in the tissues of the nerve fibers affecting their conductivity, such as Foster Kennedy has described as "pressure neuritis" in relation to tumors of the frontal lobe. There was no opportunity to examine the anatomic relations at autopsy. The character of the contraction seems to preclude any toxic element in its production, except perhaps in connection with the color defects of the visual field.

SPAETH, Philadelphia.

THE GREAT DANGER OF LUMBAR PUNCTURE IN CASES OF SUBARACHNOID HEMORRHAGE CAUSED BY ORGANIC VASCULAR DISEASE. J. G. BOROK, Monatschr. f. Psychiat. u. Neurol. **87**:184 (Nov.) 1933.

Borok observed two cases of subarachnoid hemorrhage in which lumbar puncture was followed by fresh bleeding, with fatal results. One patient had endocarditis with an embolus of the anterior cerebral artery and a hemorrhagic infarct. Two lumbar punctures were performed, three and eight days after admission. The patient collapsed and became unconscious five minutes after the second puncture, and death occurred four days later. In the second case spinal fluid was withdrawn on three occasions with marked improvement in the condition of the patient. A fourth lumbar puncture was performed four weeks after admission; within half an hour the patient became unconscious, restless and cyanotic, and he died on the following day. Necropsy disclosed a hemorrhage of the right frontal lobe which had broken into the anterior horn of the right lateral ventricle. Borok concludes that lumbar puncture is absolutely contraindicated as a therapeutic measure in cases of subarachnoid hemorrhage due to organic vascular disease. The withdrawal of spinal fluid often leads to temporary improvement, but this favorable effect is slight in comparison with the potential danger of the procedure. Lumbar puncture should be performed only when absolutely necessary for diagnostic purposes, and not more than 1 or 2 cc. of fluid should be removed. Borok also questions the efficacy of withdrawal of spinal fluid in cases of subarachnoid hemorrhage caused by trauma. In such cases he favors bloodletting by venesection as a therapeutic procedure.

ROTHSCHILD, Foxborough, Mass.

THE NATURE OF PHOTOPHOBIA. JAMES E. LEBENSOHN, Arch. Ophth. **12**:380 (Sept.) 1934.

Photophobia is a common symptom and sometimes the dominant complaint, yet attempts to explain its mechanism fail to account adequately for all the phenomena observed. By true photophobia one means that exposure of the eye to light definitely induces or exacerbates pain. It is often caused from dazzling, which is really only more or less extreme ocular discomfort. Physiologically the two conditions may be experienced simultaneously. They are, however, dissimilar. Lebensohn concludes: "With local vasodilatation as a prerequisite factor, the interplay of light, oculomotor function and sensation is necessary to evoke the pain of photophobia; blepharospasm and lacrimation result secondarily from the disturbance in sensation. That the blinking reflex is not an essential factor in the causation of photophobia is indicated by the following evidence: (*a*) In facial paralysis with keratitis e lagophthalmo, the photophobia presents the usual characteristics. (*b*) In surgical cases photophobia continues after paralysis of the orbicularis muscle and is not abolished until after the retrobulbar injection takes

effect. (*c*) In phlyctenulosis, the blepharospastic syndrome continues in complete darkness.

"The fact that photophobia is much greater with the direct than with the consensual reflex probably indicates that a fifth factor is to be considered, possibly in the nature of a direct local response to light, either metabolic or vasomotor."

SPAETH, Philadelphia.

PARALYSIS AGITANS AND TRAUMA. L. GRIMBERG, J. Nerv. & Ment. Dis. **79**:14 (Jan.) 1934.

Grimberg has analyzed critically eighty-six cases reported in the literature since 1873 in which paralysis agitans has been connected etiologically with trauma. These were the only cases in which adequate data were recorded; many of them were poorly reported but were presented by men of professional distinction. The types of trauma usually held responsible for the disease were mostly wounds and contusions. When the rush for compensation had diminished this type of trauma was greatly reduced. Many of the patients had shown tremor prior to the trauma, while others presented arteriosclerotic changes in the brain and serious psychotic manifestations before the trauma occurred. In many of the cases the trauma consisted of slight knocks, cuts, bruises, etc., which may have occurred many years before the development of the paralysis agitans.

Of the eighty-six cases, exactly half could be shown on closer analysis to have no relationship to trauma. The other forty-three cases might be used to show the possibility of such a relationship. In some cases there was a history of influenza in addition to that of trauma, and it is probable that an encephalitic parkinsonian syndrome was the result of this infection. A great majority of the cases were diagnosed on the assumption of a hypothetic neuritis ascendens, which had no existence in fact; in only two cases was there an intimate relationship between trauma and the disease, and in these the clinical picture was one of a parkinsonian syndrome due to an injury of the brain. Grimberg concludes, therefore, that trauma cannot cause paralysis agitans.

HART, Greenwich, Conn.

DIVERGENCE EXCESS. ALFRED BIELSCHOWSKY, Arch. Ophth. **12**:157 (Aug.) 1934.

In an opinion of A. Duane, expressed in 1904, nonparalytic divergent squint develops either from insufficiency of convergence or from excessive divergence or perhaps from a combination of the two. Bielschowsky has long been skeptical of the correctness of this theory. His doubts are based on both theoretical considerations and clinical experience. He thinks that there are strong reasons for the assumption of a divergence innervation antagonistic to convergence innervation. Further, the characteristic symptoms of divergence paralysis must be caused by a lesion of the divergence center or of the pathway descending from the sixth nucleus. Therefore, while declining to accept the theory of divergence excess as a general cause of divergent squint in the sense that Duane presented it, he insists on the occurrence of divergence excess as a definite anomaly with characteristic signs and symptoms.

Bielschowsky presents in detail a clinical case from which important conclusions can be drawn. First, one must distinguish passive from active divergence. Second, it is not admissible to infer overactivity of this center from an excessive prism divergence, since even in a case of passive exophoria kept in check by a strong fusion power an increased prism divergence can be found.

SPAETH, Philadelphia.

EFFECTS OF COMPRESSION OF THE JUGULAR VEIN ON THE EAR. G. A. WEILL, Rev. d'oto-neuro-opht. **11**:673 (Nov.) 1933.

It is known that pressure on the jugular vein causes congestion of the vessels of the tympanum and the drum membrane. This effect is much increased if pressure is exercised on both veins simultaneously. This sign is proposed as a test for permeability of the lateral sinus; compression on the healthy side will

show only a minimal effect if the suspected sinus is free, but the effect will be marked if the opposite sinus is obstructed. It is less well known that the compression may in certain cases produce vestibular and encephalic disturbances. Six cases exemplifying these phenomena are reported. All the patients had a disorder of the vestibular apparatus. Compression of the jugular vein produced nystagmus, vertigo and faintness or epileptic seizures, caused by congestion of the vestibule or the bulb. Queckenstedt and Riser and Sorel have shown that the encephalic mass easily becomes swollen, which increases intracranial pressure. If a point of irritation exists in the vestibular apparatus, compression of the jugular vein may produce nystagmus and true vertigo. If some alteration is present in the encephalon (the bulb), compression may determine vertiginous or pseudo-epileptic crises. Perhaps this procedure could be used to determine the central or peripheral origin of disturbances the point of departure of which is unknown.

DENNIS, San Diego, Calif.

SYNDROME OF CAUDA EQUINA RADICULITIS. FRITZ CRAMER, Bull. Neurol. Inst. New York **3**:501 (March) 1934.

A brief analytic study is presented of the case records of twenty-six patients with the typical syndrome of radiculitis of the cauda equina—fifteen cases verified by operation. The clinical and neurologic manifestations of this condition consist of: (1) a history of pain in the lower part of the back, often radiating down the lower limbs and frequently sudden in its onset, followed by progressive symptoms, with a tendency to spontaneous remissions; (2) increasing loss of power in the lower extremities, with foot drop, diminution or loss of the patellar and achilles tendon reflexes and preservation of the abdominal reflexes; (3) diminution or loss of sensation over the lumbar, and especially the sacral, dermatomes, and (4) impairment or loss of control of the vesical and rectal sphincters. Roentgen findings of marked local arthritic changes suggested a direct relationship to the symptoms of compression of the roots in 69 per cent of the cases. In 15 per cent of the cases the cauda equina syndrome was secondary to other conditions, such as sarcomatosis and Paget's disease, leaving only 15 per cent of cases which might represent a true myeloradiculitis on a toxic or an infectious basis.

KUBITSCHEK, St. Louis.

EPILEPTIC CRISES CAUSED BY A JUXTAMENINGEAL FOCUS OF INFECTION IN A PATIENT WITH OTOGENOUS CEREBRAL ABSCESS—OPERATED ON SEVERAL YEARS PREVIOUSLY. E. R. CASTELNAU, Rev. d'oto-neuro-opht. **11**:680 (Nov.) 1933.

A man, aged 40, who had recovered ten months previously from an otogenous cerebral abscess on the left side, complained one evening of a sudden attack of headache, began to talk volubly and incoherently and saw double. After a quiet night, a typical epileptic attack occurred the next morning. Irritation from a small persistent focus of infection near the meninges was suspected. The old wound was reopened, a block of fibrous tissue corresponding to the meningeal cicatrix was loosened and some granulations were removed from the former site of the mastoid antrum. Recovery was prompt. In two years there have been no more convulsive crises, and headaches have been very rare. This case must be distinguished from that of vertiginous auricular epilepsy reported by Roger and Reboul-Lachaux. The appearance of epilepsy in the course of an infection of the mastoid suggests a cerebral complication. Cases like the one reported are rare. Only two have been reported.

DENNIS, San Diego, Calif.

A CASE OF PROGRESSIVE UNILATERAL FACIAL ATROPHY TREATED WITH A MALLEABLE RUBBER PROSTHESIS IN THE MOUTH. W. BOE HILMAR, Acta psychiat. et neurol. **9**:1, 1934.

Hilmar reports remarkable results obtained in a case of severe progressive unilateral facial atrophy in a woman, aged 38. The treatment consisted of placing in the mouth a specially devised dental prosthesis made of malleable rubber so as to fill

the hollows that resulted from progressive wasting of the bone and soft tissue. The prosthesis can be molded from time to time according to requirements of adjustment. Apart from immediate cosmetic results thus obtained, the atrophic process was brought to a standstill, and in the course of time an actual improvement in the trophic condition of tissues on the affected side of the face became manifest. The integument over the forehead, cheek and chin recovered its normal color, consistency and ability to show vasomotor reactions (blushing) which previously had been lost. The condition of the bone also improved. The author attributes these effects to the stimulation of tissues by the pressure and irritation exerted by the prosthesis.

YAKOVLEV, Palmer, Mass.

EPILEPSY, TETANY AND CATARACT. H. ROGER, Y. POURSINES and M. RECORDIER, Rev. d'oto-neuro-opht. **12**:43 (Jan.) 1934.

The case is presented of a patient, aged 22, who had had epilepsy since infancy. At the age of 15 tetany appeared, and five years later an evolutive endocrine cataract was observed (the calcium content of the blood was reduced to 0.0082 Gm. per liter). Slight and variable passive hypertonia and intentional contracture of the lower limb, general muscular asthenia, nightmares and somnambulism were also present. The association of tetany and epilepsy and of tetany, spasmophilia and epilepsy have been reported in the literature. In the case reported here the epilepsy was traced to an encephalopathy, of unknown nature, occurring in infancy, as was also the dystonic subcortical syndrome; a syphilitic origin seems probable. A number of cases of an association of cataract with tetany have been reported. According to Peters, there is a lesion of the ciliary epithelium which produces a molecular concentration of the liquid of the anterior chamber and an alteration of the crystalline medium.

DENNIS, San Diego, Calif.

SEX FACTORS IN INTELLIGENCE. A. J. ROSANOFF, L. M. HANDY, I. A. ROSANOFF and C. V. INMAN-KANE, J. Nerv. & Ment. Dis. **80**:125 (Aug.) 1934.

Rosanoff and Inman-Kane studied the distribution of mental deficiency in twins of opposite sex and found that the males showed an excess of mental deficiency over the females of 29.4 per cent. Study of the sex distribution of normal or superior intelligence in twins of opposite sex was later undertaken in the public schools of Los Angeles. There was a relative excess of higher intelligence in the girls amounting to 22.5 per cent. The authors believe that the male shows greater vulnerability in the fetal state and that pathogenic factors which fall short of a lethal effect give rise among surviving children to a higher incidence of both relative and absolute mental deficiency in the male than in the female sex. Pearson's findings as to the relatively higher incidence of mental disease, crime and mental deficiency among first-born children are remarked on as illustrative of the effect of greater trauma.

HART, Greenwich, Conn.

METASTATIC CARCINOMA OF THE RETINA. JULES W. SMOLEROFF and SIGMUND A. AGATSTON, Arch. Ophth. **12**:359 (Sept.) 1934.

Metastatic carcinoma of the retina is rare. In 1926, Sattler, in his work on malignant tumors of the eye, reported what he claimed to be the only recorded case of metastatic carcinoma of the optic nerve and retina. In discussing this case, Smoleroff and Agatston think that it was not a true metastasis to the retina, but one of metastasis to the head of the optic nerve with secondary lateral spread into, and destruction of, the retina, rather than a metastasis primarily into the retina proper.

The case reported in this article is one of true metastasis of a gastro-esophageal carcinoma into the retina proper. It did not involve the optic nerve, its sheath or any other portion of the globe. The metastasis was undoubtedly blood-borne, tumor cells being present in the vessels of the lungs and liver.

SPAETH, Philadelphia.

PSYCHOANALYSIS OF MANIC-DEPRESSIVE PSYCHOSIS. C. A. NEYMANN, J. Nerv. & Ment. Dis. **80**:24 (July) 1934.

The case of a brilliant chemist, aged 37, who had suffered from eleven attacks of depression followed by elated spells is rather sketchily described with some dream material. These depict the early castration anxiety, fear of the father and an early fear of wells, holes and goats. These fears were found to be connected with an episode of the age of 3 years, in which the father allowed him to slip into an old-fashioned toilet in which the water made a great noise. The patient's suicidal attempts are interpreted as means of self-punishment for transgression of sexual laws. The sequence of the patient's depression was interrupted by the analysis, but Neymann admits ignorance of the permanent effect of the analysis.

HART, Greenwich, Conn.

PRESSURE ON THE OPTIC NERVE. ISIDORE FINKELMAN and SAMUEL WICK, Arch. Ophth. **12**:366 (Sept.) 1934.

Malignant disease of the maxillary sinus is comparatively rare. The case of Finkelman and Wick is of particular interest because the tumor extended from the maxillary sinus into the cranial cavity, causing pressure on the right optic nerve. Malignant tumors that involve the brain by direct extension are uncommon, and especially is this case uncommon in that, as rhinologists state, malignant growths of the antrum metastasize infrequently. The case was one of transitional cell carcinoma of the maxillary sinus, showing optic atrophy with choked disk and with the neuropathologic findings of increased intracranial pressure.

SPAETH, Philadelphia.

NERVE PARALYSES OF THE LARYNX OF UNDETERMINED CAUSE: THE RÔLE OF A NONSYPHILITIC VIRUS. L. BALDENWECK, Rev. d'oto-neuro-opht. **12**:31 (Jan.) 1934.

Cases of laryngeal paralysis in which the etiology is obscure are not infrequent. On the basis of a study of three such cases, Baldenweck believes that a nonsyphilitic neurotropic virus may be the causal factor. It is known that in infections with a neurotropic virus the clinical expression is variable and is often limited to a small number or even only one symptom; the onset is marked by a febrile or subfebrile episode. These infections may cause pure recurrent paralysis or associated paralysis and give rise to ephemeral manifestations or to permanent lesions.

DENNIS, San Diego, Calif.

OCULAR SYPHILIS. RALPH L. DRAKE, Arch. Ophth. **12**:583 (Oct.) 1934.

Drake discusses the presence of binasal hemianopia associated with primary optic atrophy in a case of tabes dorsalis. He reviews the literature relative to the occurrence of binasal hemianopia and also the pathologic process accounting for primary atrophy as it appears in the nerve heads. Cases of tabes dorsalis with primary atrophy of the optic nerve presenting the symptom of binasal hemianopia are also reviewed. At the same time an additional case is presented.

SPAETH, Philadelphia.

Society Transactions

NEW YORK NEUROLOGICAL SOCIETY AND NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

Joint Meeting, March 5, 1935

ISRAEL WECHSLER, M.D., *President,* in the Chair

EFFECTS OF CAFFEINE AND DEPRESSANT DRUGS ON THE HIGHEST INTEGRATIVE FUNCTIONS. DR. HAROLD G. WOLFF.

This paper was published in full in the May issue of the ARCHIVES, page 1030.

THE FUNCTION OF THE CEREBELLUM FROM A CINICAL STANDPOINT. DR. KURT GOLDSTEIN (by invitation).

The conception of the function of the cerebellum to be presented is based particularly on clinical considerations. The theory, developed on the basis of many observations, is simple. The cerebellum supports motor performances innervated by higher levels, particularly voluntary purposeful acts, by a kind of coinnervation. The motor acts as determined by the whole organism may be maintained automatically if the situation demands it. Lesions of the cerebellum produce two groups of symptoms: (1) positive symptoms—phenomena consisting of abnormal exaggerated reactions of the organism to stimuli, induced by unusual activity of the subcerebellar apparatus brought about by its isolation and release from cerebrocerebellar control—and (2) negative symptoms—asynergia, asthenia, disturbance of tone, changes in muscle innervations and disturbance of balance.

The positive symptoms consist of overactivity of the labyrinth and other sense organs, noted particularly in an increase of falling, deviation, etc., on stimulation of the affected side, in an abnormal "turning to" tendency of the subject toward the source of the stimulation, a particular expression of which is abduction and extension. This tendency becomes manifest in different symptoms, as in past pointing, deviating and falling, which usually occurs in an outward direction, i. e., away from the body. Moreover, different symptoms of disturbed sensibility appear particularly in the realm of localization. In normal subjects the effect of environmental stimulation is equally strong on the two sides of the body; the consequence is a state of equilibrium. In cases of cerebellar disease the effect is more marked on the affected side; the patient is drawn to that side and hence falls, deviates and past points. The past pointing, deviating and falling proceed only to a point a certain distance away from the midline of the body. At this point the limb is motionless. This is caused by the abnormal tendency of persons with cerebellar lesions to *ausgezeichneten Verhalten,* i. e., to assume the best posture (*Deutsche Ztschr. f. Nervenh.* **109**:1, 1929). The normal person has such tendencies also. However, he is able to choose uncomfortable attitudes, because of the innervation of the forebrain and the coinnervation of the cerebellum. In persons with cerebellar lesions this inclination to maintain comfortable attitudes appears to an abnormal degree. It is expressed in unusual positions of the head, arms and legs in abnormal and voluntary movements, when the patient puts his limbs into an uncomfortable position, and in other symptoms.

The abnormal tendency to extension and abduction is caused by a lack of cerebellar coinnervation, which normally favors movements of flexion and adduction particularly, as demonstrated by different facts, viz., the effect of stimulation of the cerebellum and the cerebrum which is especially apt to produce flexion and

adduction, the diminution of decerebrate extensor rigidity by stimulation of the cerebellum, the guiding rôle which flexor movements play in alternating movements and the fact that flexor movements are the essential features of complicated finely executed motor acts. Decerebrate rigidity is caused by interruption of the connection between the forebrain and the subcerebellar apparatus. The tendency to extension and abduction in cases of lesions of the cerebellum may be regarded as a slight form of extensor rigidity with defects in the flexor performances.

In the normal organism the cerebrocerebellar and the subcerebellar apparatus work together to guarantee the exact execution of movements and postures. In cases of lesions of the cerebellum the extensor performances are in the foreground and the flexor performances are inadequate.

The negative symptoms are regarded as caused directly by the lack of coinnervation of the cerebellum and defective utilization of cerebellipetal stimuli and indirectly by the disturbances brought about by positive symptoms.

From a consideration of the different negative symptoms the conclusion is reached that the cerebellum need not be viewed as a coordinating organ. Finally, it may be stressed that this theory is in best accord with the anatomic facts and is not only best fitted to explain the known symptoms but helpful in pointing the way to new ones which may be important for the diagnosis of cerebellar disease.

DISCUSSION

Dr. Charles A. Elsberg: I am especially grateful for the declaration that the cerebellum must not be looked on as a separate organ controlling motility in some other organ, but that there is one large motor organization in which supratentorial, cerebellar and subcerebellar structures each play their part. I should like to know exactly what Dr. Goldstein means by the subcerebellar apparatus. Of course, as he stated, he is going back to a considerable extent to the original views of Luciani, who declared that the activity of the cerebellum is not one sui generis but rather an activity common and, so to say, fundamental to the whole motor organization of the central nervous system.

The theory of cerebellar activity which Dr. Goldstein has presented is alluring and perhaps has much to support it. Certainly it is important to appreciate that the cerebellum has an important influence on movements of flexion and adduction and that when the functions of the cerebellum are disturbed primal abduction and extension occur. Most neurologists probably think that when a patient with cerebellar disease stands with his limbs wide apart or walks on a broad base he is doing so in order to give himself better support. According to Goldstein's theory, normal adduction and flexion have been interfered with, and therefore abduction and extension occur. I cannot follow Dr. Goldstein in his point of view, if I understood it correctly, that decerebrate rigidity is an evidence of this primal extension and abduction. Of course it is true that removal of the cerebellum will increase decerebrate rigidity and that stimulation will diminish it, but I am not at all certain that this signifies that decerebrate rigidity is an extension phenomenon due to lack of cerebellar control.

I am in full accord with Dr. Goldstein's statements regarding what he calls the negative and positive symptoms in cases of cerebellar lesions, although it is not quite clear to me exactly what areas he includes in the subcerebellar apparatus. In spite of the mass of clinical and experimental investigation that has been made, it is still not at all clear why, for example, in total agenesis of one cerebellar hemisphere, or of one and much of the second cerebellar hemisphere, there may be few if any discernible disturbances of the so-called cerebellar type. It may be, and I think Dr. Goldstein intimated as much, that available methods for examination of cerebellar function are really very gross, as are most methods for the examination of motor or sensory function, and that in the future more refined tests must be devised.

I was greatly interested in Dr. Goldstein's remarks concerning hypotonia, and in his statement that hypotonia is likely to be marked in cases of acute cerebel-

lar lesions and is not easily demonstrable in cases of chronic or slowly progressive lesions. In this respect his experience has been different from mine and from many of those who see cases of cerebellar disease in which surgical intervention is necessary. I have never seen as striking an instance of hypotonia as in the very slowly progressive disturbances produced by meningioma in the posterior cranial fossa. In my experience patients with such a condition often have very marked hypotonia in the advanced stages of the disease. On the other hand, if a considerable part of the cerebellum is removed by the surgeon or destroyed by the operative procedure, it is often astounding that there are very few, if any, disturbances of the cerebellar type after the first few days. Dr. Cushing made the statement that a large portion of a cerebellar hemisphere can be excised without causing any disturbance, and this has been the experience of all neurologic surgeons. I have seen hypotonia again and again in patients with slowly progressive lesions of the posterior fossa, expanding in nature, and have noted its absence in patients who had very acute lesions. Of course, as Dr. Goldstein said, in "cerebellar shock" as in all shock of the central nervous system there may be loss of cerebellar function as well as loss of all tendon reflexes.

Many of the problems of which Dr. Goldstein has spoken and those to which I have referred are still unsolved.

Dr. Henry Alsop Riley: I feel that Dr. Goldstein has contributed materially to knowledge of the cerebellum by his paper. I had the opportunity of reading it, and to me the principal difficulty was that many of the things which Dr. Goldstein emphasized are rather unusual in my experience. I would naturally conclude that was due to my lesser experience, but I feel that while the expression of his theories is stimulating, there still is a great deal of clinical and anatomic evidence which makes me inclined to cling, at least for a time, to the old conception of the cerebellum. As Dr. Elsberg has said, it may well be that by calling attention to these matters Dr. Goldstein will succeed in making one more keen and observant in noticing these signs which he perhaps more than any one else has studied. It has seemed to me that the function of the cerebellum is definitely twofold; this is based on the evidence of comparative anatomy. The anatomic structure of the cerebellum cannot fail to convince one that its function is twofold: an old function which goes all the way back to the very origins of the phylogenetic scale concerned with equilibrium and a more recently acquired synergic activity. I was not entirely certain after reading Dr. Goldstein's paper whether he meant to minimize as much as I thought he did the equilibratory activity of the cerebellum. The synergic activity is one which emerges with the development of the independence of the limbs and is accompanied by a progressive expansion of the middle portion of the cerebellar hemisphere, which shows a graded and progressive advance, particularly in the primate group, into its completion in lobulus C of man.

I was at a loss to understand Dr. Goldstein's reference to past pointing. It certainly is true that past pointing is usually in an outward direction, as tested in the ordinary way, but it seems a little dangerous to postulate cerebellar activity in outward past pointing and vestibular activity in inward past pointing; it seems that the whole function of pointing is so closely unified that the segregation of the function outward in the cerebellum and inward in the vestibular apparatus is difficult to understand.

In considering the general organization of motor patterns, movements of flexion are not always more powerful; they are in flexion of the forearm on the arm but not in the lower extremities when compared with extension of the leg on the thigh. Complicated activities are performed not by flexor and adductor muscles but by a very finely graded correlation of physiologic synergists. Just as much accuracy is required of the extensor as of the flexor muscles in prolonged succession movements, such as the execution of trills in playing the piano or violin, although the dominant action of the flexor muscles requires more strength. If either flexion or extension is inaccurate or incoordinate, the skilled act is destroyed. The production of the arches, slings, little

hooks, etc., mentioned by Dr. Goldstein, must require as carefully graded control of the extensor and abductor muscles as of the flexor and adductor muscles.

It is not entirely clear how Dr. Goldstein separates the activity of the cerebrocerebellar apparatus, which he states is to a greater extent decided by the will, from that of the subcerebellar apparatus activated by external world stimuli. The cerebral apparatus is so patently influenced by the external world stimuli that the significance of this statement is not clear.

Questions of hyperexcitability of persons with cerebellar disease are not supported by my experiences with adults and children with neoplasms of the cerebellum. The examples given of increased excitability on the affected side in response to stimuli of light and sound, in particular, are difficult to understand in view of the exquisitely bilateral distribution and representation of the centers for light and sound reception and perception.

I have had no experience with the exaggerated "to-turning" phenomena; so I cannot discuss this phase of the subject. It is hard to understand the applicability of the "to-turning" tendency with falling, deviation, etc., which are distinctly connected, at least in my mind, with the equilibratory function of the cerebellum. In my experience the past pointing in cerebellar disease continues to increase until the deviation is such that a very material alteration in stresses and strains occurs which cannot help but stimulate the kinesthetic sense, which then tends to correct the deviation by other, perhaps higher, mechanisms. I similarly have made no observations on the inability or disinclination of the patient to maintain assumed uncomfortable positions; so I have no first-hand knowledge of these phenomena, but I do not see the exact connection between the facts and the theory. Not all movements of flexion or adduction are easier to maintain or more comfortable to assume than movements of extension and abduction.

I agree that asynergia, hypermetria and disturbances in the finer control of muscle integrations are dependent on cerebellar disease, a disruption of the synergic unit, a defective and insufficient coinnervation, together with abnormal activity of subcerebellar centers. Every one will agree that the organization of skilled acts requires the most perfect coordination of all the motor centers through a centrally organized motor pattern. The cerebellum is only a collaborator in a most highly organized system, requiring perfect cooperation from all the integrated units. Lack of correct coinnervation must certainly be accepted as an expression of defective cerebellar contribution. If synergy fails in a case of cerebellar lesion, the process of producing synergy must be considered as supplied by the cerebellum.

I agree entirely with Dr. Goldstein's remarks on localization. Except in major subdivisions and in particular forms, I can see little indication of discrete localization in the cerebellum. The remarkable development of the paraflocculer and flocculer formations in the various types of aquatic mammals seems without doubt to indicate that these parts are particularly endowed with the integration of the muscular control underlying the movements of the body, limbs and tail.

No one can too emphatically endorse the conception with which Dr. Goldstein closes his paper, i. e., that each part of the nervous system is not a solo player in the nervous orchestra but only a highly endowed trained cooperator and collaborator in a total function.

DR. KURT GOLDSTEIN: I am sorry that I was unable to demonstrate the symptoms about which I have spoken either on patients or by moving pictures which I have brought from Germany. Such demonstration alone would make it possible to discuss the theory which is based on the whole symptomatology, and particularly on some symptoms which are not so well known but to my mind very important. I might mention that the facts are described in a paper published in the "Handbuch für normale und pathologische Physiologie" (1928, vol. 10, p. 223).

It would take too long to answer each point of the discussion, but I should like to answer some of Dr. Elsberg's questions. I think there is a misunderstanding. If I say that patients with acute cereberallar lesions have hypotonia, I refer to

patients with diseases which damage the cerebellar cortex severely, for example, acute injuries. In such cases Gordon Holmes (*Brain* **40**:461, 1917) described hypotonia. I believe that hypotonia is often found only by special examinations.

What I mean by the subcerebellar apparatus I have already pointed out. This apparatus is connected especially with the cerebellum and not directly with the cerebrum. Therefore, this apparatus is not directly under the influence of the will.

Certainly I do not deny the great importance of the cerebellum for balance, synergia, coordination of movements, etc. I differ only in the explanation of the way in which the cerebellum deals with these performances. I believe that the cerebellum, important as it may be, plays only a dependent rôle in these performances, namely, by coinnervating supracerebellar conditioned innervations (under the influence of cerebellipetal stimuli). About this special function of the cerebellum I believe I would come to an agreement with Dr. Riley if we could discuss the different points which he mentioned in patients. Regarding the questions of the differences between flexion and extension, I believe there is a misunderstanding. Certainly I also suppose that all performances are executed by flexor and extensor movements, but the rôle of the flexor and extensor movements is not the same in all performances in some the flexors are leading in others, the extensors. I prefer to speak of flexor performances, not movements. I believe that flexor performances are under the influence of the cerebrum and cerebellum to a greater extent; and extensor performance, under the influence of the so-called subcerebellar apparatus.

A word about the connection between the patient's difficulty in maintaining uncomfortable positions and the other symptoms. The maintenance of uncomfortable positions is normally guaranteed by the influence of the forebrain and the coinnervation of the cerebellum; so the patient's inability or the difficulty in this respect is also caused by the lack of coinnervation.

For another reason the consideration of these phenomena seems to me important, because only thereby may it be possible to understand the symptoms in man or animals with cerebellar lesions. These symptoms are caused by the disturbed function of the cerebellum and by the new adaptation which is designed to find a new "best behavior posture" in spite of certain changes.

ESSENTIAL HYPERTENSION: A REPORT OF THE RESULTS OBTAINED BY BILATERAL VENTRAL RHIZOTOMY (SIXTH THORACIC TO SECOND LUMBAR ROOT) AND BILATERAL RESECTION OF SPLANCHNIC NERVES. DR. ALFRED W. ADSON (by invitation).

Essential hypertension is the result of excessive or abnormal vasopressor reactions. The disease may occur at any age, but it occurs most frequently in the second, third and fourth decades of life. Examination of the retinal arteries and biopsy of muscles reveal vasospasm with muscular hypertrophy in the arteries and arterioles before sclerotic changes appear. Ultimately the cardiovascular-renal mechanism succumbs to the excessive burden, and premature death results.

Sudden and abnormally high rises in the blood pressure of apparently normal persons suggest one of two faults: that the vasomotor response is due either to sudden mobilization of vasopressor substances or to a hypersensitive vasomotor mechanism. I am of the opinion that essential hypertension results from a combination of these faults. If vasopressor substances are chiefly responsible for increases in blood pressure, subtotal resection of the adrenal glands should greatly relieve the symptoms. If, however, such increases in blood pressure are due to a hypersensitive vasomotor mechanism, better results would be obtained by extensive ventral rhizotomy or by resection of the splanchnic nerves.

Although favorable reports have been given on subtotal resection of both adrenal glands in the treatment of essential hypertension, a review of the experience at the Mayo Clinic in 32 cases indicates that major operations on the nerves are most effective and that bilateral ventral rhizotomy, through a laminectomy wound, from the sixth thoracic to the second lumbar root, inclusive, is more effective than bilateral resection of the splanchnic nerves. However, bilateral resection of the splanchnic nerves, with removal of the first and second lumbar sympathetic

ganglia on each side, with or without subtotal resection of the adrenal glands, will probably be just as effective as extensive rhizotomy.

The object of rhizotomy or resection of the splanchnic nerve is threefold: (1) to denervate a large vascular field, thus decreasing the number of vessels capable of going into spasm, (2) to create a blood reservoir in the denervated vessels and (3) to remove all influence of the sympathetic innervation to the adrenal glands, thus blocking central impulses that might call for a sudden discharge of additional epinephrine.

The mean drop in systolic pressure after extensive rhizotomy was 44 mm. of mercury, while the mean drop in diastolic pressure was 38 mm. These pressure readings were taken one month or more after operation, since immediate postoperative readings do not reflect the true status of the blood pressure, as they are much lower than readings taken after the patient has fully recovered from the operation.

Patients who have responded best to such major operations on the nerves are those who have been in the earlier phases of the disease. They are persons whose symptoms of hypertension are progressive and who do not respond to medical measures but whose disease has not done irreparable damage to the heart, kidneys and retinal and cerebral vessels. The operation must be performed before the blood vessels become sclerotic and fail to relax following denervation.

Bilateral resection of the splanchnic nerves was performed in 7 cases. In 2 cases good clinical results were obtained with only a slight drop in blood pressure. Bilateral ventral rhizotomy was performed in 22 cases. Excellent clinical effects, with sustained lower levels of blood pressure, resulted in 9 cases. Only fair results were obtained in 6 cases, whereas 3 patients failed to obtain relief and 2 died following operation. One of these 2 patients succumbed to meningitis (hemolytic streptococcus) and the other to cardiovascular failure. Two patients are still convalescing from the operation; sufficient time has not elapsed to draw definite conclusions, but the prospects appear favorable.

Three additional patients with essential hypertension have had the following operations: In 1 case, that of a man aged 55, the intercostal nerves supplying the abdominal muscles were divided in order to study the effects of abdominal pressure. The result was disappointing. The systolic blood pressure fell 20 mm. of mercury when the patient assumed the upright position. This fall in blood pressure, however, was not sufficient to give the patient any clinical relief.

The second patient presented a complex group of symptoms simulating those described by Cushing under pituitary basophilism, but in the light of Dr. Walter's experience in removing tumors of the adrenal glands and hyperplastic portions of the adrenal glands in similar cases it was agreed that both adrenal glands should be explored. No tumors were found. The right adrenal gland was removed, and the one on the left was resected, leaving about two fifths of a normal gland. The result was disappointing in that the patient presented signs of adrenal deficiency which necessitated the administration of extract of the adrenal cortex and sodium chloride. The blood pressure promptly rose to the preoperative level on administration of these substances, and the symptoms of so-called pituitary basophilism did not disappear.

The third patient was a high school superintendent, aged 46, who presented the classic symptoms of essential hypertension. Instead of performing the extensive rhizotomy, which includes the anterior roots on both sides from the sixth thoracic to the second lumbar vertebra, inclusive, I chose to increase the scope of the operation on the splanchnic nerves, and on Feb. 19, 1935, employed a left renal incision, which was extended upward to allow resection of the twelfth rib on the right side in order to facilitate exposure of the upper retroperitoneal space. The incision allowed the insertion of a broad illuminated retractor which displaced the liver, kidney and perinephric fat capsule anteriorly. This in turn gave ample exposure of the splanchnic nerves as they perforated the diaphragm and entered the celiac plexus. It also permitted exploration and elevation of the abdominal vena cava so that I could resect the first and second lumbar ganglia and inter-

vening trunks, thus interrupting the fibers that descended from the twelfth thoracic sympathetic ganglion. It also permitted complete severance of the white rami which communicate with the first and second lumbar ganglia on each side. This latter addition is probably significant, since these white rami represent the lower end of the thoracolumbar outflow and contain numerous preganglionic fibers that not only innervate the adrenal glands but carry vasomotor impulses to the splanchnic vessels also. The patient's convalescence following an operation on the right side was uneventful and satisfactory. The complete results cannot be evaluated, however, until a similar operation has been done on the other side. It is barely possible that this extensive surgical procedure may supplant the extensive rhizotomy through a laminectomy wound. Furthermore, if resection of the splanchnic nerves and removal of the sympathetic ganglia and trunks were insufficient, it could readily be combined with subtotal resection of each adrenal gland.

DISCUSSION

DR. GEORGE J. HEUER (by invitation): Dr. Adson and his colleagues have originated some procedures and have followed measures suggested by others until their experience now embraces most of the methods described for the surgical treatment of hypertension. One of their most valuable contributions, I think, has been an effort to classify cases of hypertension, so that one may in the future more accurately compare the results of different methods of treatment. Dr. Page and I have been interested in the subject of surgical treatment in these cases, and while we have not had the experience available to Dr. Adson and others at the Mayo Clinic, we now have 10 patients with essential hypertension treated by division of the anterior nerve roots. Our results, due no doubt to a better selection of early cases, are favorable in a higher percentage of instances, for we have had good results in 8 of 10 cases.

At the present time discussion of the subject of essential hypertension and its treatment by adrenalectomy, adrenal denervation, resection of the splanchnic nerve and section of the anterior nerve roots is made difficult because of the fact that greater care has not been exercised in diagnosis in the cases in which surgical intervention was performed. I have recently completed a survey of the literature on the subject, and I am not convinced that all of the patients subjected to operation had essential hypertension; the probability is that many of them had hypertension secondary to chronic nephritis. Not only is there a question concerning the diagnosis, but it is not always clear at what stage in the disease the operation was performed. I have no doubt, as Dr. Adson indicated, that it will become increasingly evident that an important factor from the standpoint of results is the stage of the disease in which operation is undertaken. One must also establish criteria as to what constitutes a satisfactory result. There are reports in the literature of cases in which following some surgical procedure the patient was relieved of slight headache and the result of the operation is recorded as good, although the blood pressure had not been affected. The subject is fascinating, but it requires elucidation. I think surgeons are on the right track even though, at present, one does not understand the exact cause of the disease.

PHILADELPHIA PSYCHIATRIC SOCIETY

Regular Meeting, March 3, 1935

JOSEPH C. YASKIN, M.D., *President, in the Chair*

PARANOIA WITH FOLIE À DEUX. DR. JAMES GREENWOOD.

True paranoia, which according to the kraepelinian definition is a "fixed type of disease, due exclusively to internal causes and characterized by persistent

systematized delusions, the preservation of clear and orderly thinking and acting and by absence of hallucinations," is indeed a rare mental disorder. I shall present a patient with a condition which, while I hesitate to label it definitely true paranoia, shows many features which lead to a diagnosis of a paranoid condition closely approximating paranoia vera. With the patient is one of his disciples or followers who has, I believe, folie à deux.

CASE 1.—C. T., a Negro aged 46, was admitted to the Philadelphia General Hospital on Feb. 7, 1935. This was his second admission. His past history is significant. He was born in Pennsylvania and reached the eighth grade in school. His family were Baptists. He was always religiously inclined and was baptized at the age of 13 and became superintendent of his Sunday school several years later. At the age of about 20 he married. It is alleged that for a number of years at a later period he lived with another woman, but he subsequently returned to his wife. One child was born of this union, who is mentally defective at the moron level. The patient has never drunk or gambled. About sixteen years before the present admission he began to believe that people should refrain from sexual intercourse, which he considered sinful, and that women could conceive immaculately, thus maintaining the race. He and his wife practiced continence according to his belief, and he founded the Unity Bible Class of Philadelphia so that others could learn of these revelations. His class grew, and he had a number of followers, mostly women. They worked, pooled their funds and increased their earnings by singing at churches. They established a house called the "Saints' Retreat," where a number of women members lived. The patient and his followers believed that a child born of the normal relationship between man and wife was born in sin and that the wages of sin is death, while the gift of God is eternal life, and that woman can conceive immaculately. The followers were expected to refrain from what their leader believed to be sinful. By 1932, 8 children had been born to the women who lived in the Saints' Retreat, and the patient looked on them as being born of the seed of woman alone, for which the Lord was responsible.

By 1932 the patient had been the "father" of his religious cult for thirteen years. In June 1932 the Society to Protect Children from Cruelty received a complaint that a minor was housed in the Saints' Retreat and that the patient had had improper relations with her. There was no proof of this, as none of his followers gave information pertaining to improper advances made by the "father," but the house was raided and a number of Negro women were found to be living there with eight children. The patient, with his assistant, C. J., was arrested and arraigned in the morals court. The judge decided that an immoral house was being conducted in the guise of a religious organization, and since no biologic or legal explanation of the birth of the children was forthcoming and the court was not satisfied with the theory of immaculate conception, both men were sent to the Philadelphia General Hospital and were subsequently committed to the Philadelphia Hospital for Mental Diseases on July 28, 1932. Both the patient and his assistant maintained that they had abstained from intercourse for thirteen years.

While hospitalized the patient showed little in addition to the beliefs recorded. He was pleasant, agreeable and respectful and gave an accurate story of his life. He was well oriented, showed no memory defects and had no hallucinations. His beliefs were fixed and were backed up by lengthy biblical quotations, which he interpreted literally. The "original sin" of Adam was frequently referred to, and the Book of Revelations furnished much of the foundation for his ideas. His intelligence was apparently high, and his general information good. He had been arrested once on the charge of a white member of his Unity Bible Class who said that he was the father of her child. He denied this, saying that he had refused her advances because he did not believe in sexual intercourse. He would admit no possibility of his being of unsound mind but expressed no resentment on being questioned on the subject. Physically, he was well developed and of short stature and presented no abnormalities. Serologic tests of the blood and spinal fluid were negative.

In the hospital he was quiet, cooperative and a good worker in the kitchen. He was accordingly given many privileges. On Jan. 15, 1933, both the patient and the disciple, C. J., escaped. He soon reorganized the religious group. Two years later he was readmitted to the hospital (Feb. 7, 1935), once more being charged with running a disorderly house. His beliefs are exactly as recorded three years before; his following still includes most of the original members and his assistant was again arrested with him. Four more children had been born in the interval, bringing the total to 12. There has been a slight elaboration of the delusional system; he now says that the original sin of woman (sexual intercourse) is punished by loss of menstrual blood, which contains life, and that if she is able to retain the flow she can conceive immaculately. This, he says, has happened to several women in his Bible class. He is reasonable enough to admit the possibility that the women may have slipped from his teachings, but he does not believe this to have occurred.

CASE 2.—C. J., a Negro aged 36, single, was admitted to the Philadelphia General Hospital on Feb. 7, 1935 for the second time. There is little of significance in his family history. He was born in Pennsylvania, was always healthy and reached the seventh grade in school at 14 years of age. He worked in a lumber yard for four years and later obtained steady work as a janitor. About sixteen years ago he joined the Unity Bible Class founded by the first patient and became a firm believer and a faithful follower. He believes that God intends that propagation of the human race will be eventually by immaculate conception alone. He has abstained from all wordly relationships since he joined the "class" and has not been at all troubled by abstinence, since he found joy and fulfilment in striving to pattern his life according to the doctrines and beliefs of the "father" of the Unity Bible Class. He frequently visited the Saints' Retreat and lived there for a while. He was arrested with his leader in July 1932.

This man was quiet, agreeable and cooperative. He was well oriented and showed no memory defects. There were no hallucinations. His delusional beliefs were identical with those of the first patient. He appeared to be deeply religious, quoting somewhat more crudely from the scriptures than his leader. He was less inclined to be systematic about these things, and his reasoning was not as good. The scriptures were frequently invoked to back him up, and often he would say merely, "It's in the scriptures." There was a tendency to exaltation when he discussed religious matters, and he said that he was a prophet. He accepted his incarceration as part of the life of a religious man. Physical examination revealed no abnormalities. Laboratory studies, including serologic tests of the blood and spinal fluid, gave entirely negative results.

When he was returned to the Philadelphia General Hospital on Feb. 7, 1935, there had been no change in his beliefs. He is somewhat reluctant to discuss his religion and shows some apathy. Systematization is again not perfect. He does not understand why the public looks with disfavor on his religion or why the police should make attempts to suppress it. He blames the difficulties on one person, a woman who is opposed to the organization and is herself a sinful person.

Comment.—Of the first patient, I can say that he is sincere, honest and really lives the life of which he speaks. His emotions are in keeping with his thought content. He is quiet and religious, making no effort to push himself to the front, at least not in the presence of physicians. He accepts his incarceration with tolerance and believes that it is the result of a misunderstanding. He does not expect his belief in immaculate conception to be immediately accepted, nor does he believe that immaculate conception will become universal for many years. He only asks that he be allowed to teach so that more and more people will be led to believe the truth as he does himself. He possibly has true paranoia; the second patient, folie à deux.

DISCUSSION

DR. O. S. ENGLISH: I think that the first patient has a paranoid condition, which perhaps approximates paranoia vera, although he expresses himself illogically

at times and is rather incoherent; one has the impression that he has not a good grasp on reality. The second patient mirrors and echoes the beliefs of his leader. The belief is almost entirely an effort to renounce sexuality, or at least heterosexuality. That raises the speculation whether there is any homosexuality between these two. I am not sure of his veracity, although I am open-minded about it. I wish to ask Dr. Burr if it is likely that paranoid schizophrenic patients would prevaricate as much as would hysteric or amnesic patients.

Dr. Charles W. Burr: I am sure that the first patient has not the slightest idea what the term "immaculate" and "conception" means. He is grossly ignorant, though with considerable intelligence for his race. He has been reading the Bible, a book which for centuries was kept from the ignorant lest they get into trouble, and has built up a whole crop of false biologic ideas. Sex and religion are always tied closely together.

As a rule, the paranoiac patient is also homosexual. I cannot recall a case of paranoia in which I really knew the conduct of the patient and did not discover that he was homosexual. I think that it is part of the picture of paranoia. If one really knew the history of these men, I believe that one would find that both are homosexual, or rather bisexual. If some man attracted them they would probably show homosexual tendencies, and it is probable that when no women are present these men have relations with each other. As to lying, mental disease does not make a man truthful. Manic patients will often lie to make fun of one. The person with paranoia will lie for a motive, to gain his own way. The only psychotic patients that I know who do not lie are those with true involutional melancholia. The leader of this cult would convince one plausibly that it is justifiable to lie in order to convince others of what he is trying to preach. These men are dangerous and should be segregated permanently.

Dr. Baldwin C. Keyes: I do not agree entirely with Dr. Burr as to the disposition of these men, and question whether they have true paranoia. I think that they come closer to the group of superstitious Negroes who convince themselves of certain facts which they can make useful to themselves, and are sufficiently eloquent to convince others. They are willing to accept other explanations guardedly. If they get into trouble they are somewhat willing to change their beliefs in order to avoid the consequences. The second man has been a follower for seventeen years. I happened to see most of the women from the Retreat. The judge questioned them one after the other and received for the most part the same statement. They were proud and perhaps exalted and said that the light of the Lord had passed over them and they had become pregnant. They swore that they had never had sexual relations. They were in a comfortable house; they lived a club existence. They went out to work, while one woman was appointed to take care of the children. The group pooled their funds. One cannot blame them for accepting beliefs that gave them such a comfortable living. I think that one need place them in an institution only if this recurs.

Dr. Frederic H. Leavitt: A third member of this cult, a woman, was in my service at the Philadelphia General Hospital. I questioned her at length several times. She accepts in parrot-like fashion the beliefs of the leader. She has shown no mental aberration. In Philadelphia one cannot help but be impressed by the number of these religious cults that have opened in the Negro sections during these hard times. I have noted six or seven such places—the House of God, the House of the Redeemer and Saints' Rest. They are scattered over the city, particularly where Negroes congregate.

Dr. William Drayton: I talked with about twelve of the children from this group; they were among the best brought-up children I have seen and were the neatest and cleanest. In the morals court, where they spent one whole day, none of them fought, tried to steal anything or created any commotion; they merely sang spiritual songs. The children were well taught; one of the women had been a kindergarten teacher. One of the children, aged 10 months, could keep time to

music. There is no reason why these people should not be returned to society; they were not doing harm to any one. Now they are all subjects of relief.

DR. S. F. GILPIN: There is a great difference between the two patients. If there ever was a case of paranoia vera, the first man has that condition; he soars above the mind of the ordinary man. The other man, I think, was making a good thing out of the situation, believing the doctrines because it suited him. He has good insight. The first man argued just the same tonight as he did the first time he expressed these ideas. I think that he is entirely different from his pupils. The woman believes his ideas; she does not know why; she has not analyzed them. She makes many statements in which nothing is clear; she does not realize what she is trying to tell. I suppose that may also be true of other members of the class.

PSEUDOCYESIS. DR. FREDERIC H. LEAVITT.

A Negro woman, aged 36, came to the outpatient department of the Philadelphia General Hospital, stating that she was pregnant. A pelvic examination revealed a normal nongravid uterus, no enlargement of the abdomen or breasts and no other signs of pregnancy. The patient believed that she was at term, despite the fact that she had menstruated regularly each month and there had been no increase in the size of the abdomen. She was transferred to the psychopathic department of the hospital for observation. There she said that she had had one child, aged 21, and that her great desire had been to have more children; she had not been able to achieve that ambition. She persisted in the statement that she knew she was pregnant and was about to be delivered. She was euphoric, cheerful and seemed greatly pleased. She was jocose, silly, somewhat grandiose and inconsequential in her behavior and statements and showed evidence of mental deterioration in that she was unable to retain ordinary facts, names or figures in memory and would fail to answer questions that required an ordinary degree of intellectual ability.

Physical examination revealed signs suggestive of dementia paralytica: slurring of speech, smoothing out of the facies, tremor of the tongue, fingers and lips, unequal pupils, exaggerated knee jerks and a general mental attitude that one associates with this disease.

The case is regarded as one of dementia paralytica with pseudocyesis as a result of transference into a delusion through the medium of wish fulfilment—a consummation of a desire that she had had for over twenty years. There is no history of alcoholism or of treatment for syphilis. A Wassermann test of the blood and spinal fluid was negative; the results of the colloidal gold test have not been reported.

DISCUSSION

DR. JOSEPH YASKIN: Was the patient addicted to the use of bromides?

DR. FREDERIC H. LEAVITT: There is no history of the use of drugs or any record of treatment because of their use.

THE PSYCHOPHARMACOLOGY OF SODIUM AMYTAL IN CATATONIA. DR. MELVIN W. THORNER.

Careful study reveals that the various layers of the nervous system are affected successively by increasing concentrations of sodium amytal; the order in which the layers are affected is in consonance with the phylogenetic development of the functions of these layers.

The conclusions reached are: (1) that sodium amytal acts partly by inhibiting the activity of the nerve cells; (2) that the various divisions of the nervous system are affected in the order of their phylogenetic appearance, i. e., the latest are the most easily affected; (3) that the "release phenomena" observed may be explained by the inhibition of higher inhibitory centers, and (4) that in the overinhibited catatonic states sodium amytal exerts specific psychologic effects.

DISCUSSION

DR. KENNETH E. APPEL: This work continues a tradition in psychiatry that comes from Switzerland and has been carried on for many years. It started with Greisinger and was continued by Klaesi and Oberholtzer at Bleuler's clinic and in this country by Lorenz and Palmer, Lindemann and others. It represents a chemical attack on mental disease. After reading Dr. Thorner's paper three types of reflections occurred to me—therapeutic, psychopathologic and organic and structural.

Dr. Thorner has spoken of the therapeutic results and the advantages of obtaining insight into the mental activity of patients. In that sense he has followed Palmer and Lindemann, who reported increased accessibility and cooperation. Information of value is secured with the use of the drug. This unquestionably has therapeutic possibilities that have not been followed to the fullest extent. I know of no report in the literature of the administration of sodium amytal with the continuous application of psychotherapy for weeks to a patient who was uncooperative and yet could be made cooperative with this drug. Since catatonia and mutism can be decreased temporarily, how can this be made permanent? It is not impossible that this problem will be solved. At the Pennsylvania Hospital results have been much better in cases of manic-depressive mania than in cases of schizophrenia. Does the drug release inhibitions? In manic cases it seems to increase inhibitions, which also has therapeutic value. What is the mechanism of the good therapeutic results? Bancroft's colloidal conceptions do not help. Is it that the narcosis or deep sleep allows a long rest period—a prolonged anabolic state—which leaves the organism fresh at the end of it, and with more energy to tackle life again? Is it a purely chemical or metabolic process? Is it partly psychologic, a respite from conflicts and difficulties? Is it a breaking up of unfortunate psychologic associations? Is the forced dependency an important factor of psychologic significance? Experience at the Pennsylvania Hospital seems to indicate that the enforced dependency is of definite psychologic importance. The greater the prostration when these patients come out of the condition, the greater the dependency. Dr. Kelman, following Dr. Solomon, has spoken of the therapeutic importance of the increased attention which the patient receives when he is under purely chemical treatment with carbon dioxide.

The second set of reflections concern psychopathologic aspects. The drug throws light on the psychology and the disease process in many cases. Beneath the blocking, one finds that a mind is present, with more normal associations, more affectivity and more rationality than one usually suspects or can readily discover or reach. The therapy therefore throws light on psychopathology and the structure and dynamics of the mind. As such, the use of this chemical approach to mental disease should give much hope that a method or substance will be discovered which will restore permanent accessibility, cooperation and normal functioning. A whole group of drugs will produce this result; carbon dioxide is one. Pascal and Deschant reported that caffeine and ether have the same effect. They have tested many drugs and showed that if large enough doses are given inhibitions are broken down and the patients become accessible. Another such drug is bulbocapnine. Hill reported beneficial effects in postencephalitic behavior disorders from the administration of this drug. In animals it produces catalepsy, and in man akinesis and a sort of imitation parkinsonism.

This brings me to organic considerations. There are probably close relations between schizophrenia and encephalitis—the lethargy and the dreamlike state, the rigidities, the automatic movements, etc. Toulouse and Rottenberg called attention to the similarity of the mental state in certain cases of encephalitis and of schizophrenia. There are also neurophysiologic studies which facilitate or visualize organic correlations. That the area responsible for sleep is between the mamillary bodies and the nucleus of the third nerve was hypothecated by Economo. Ranson has shown that lesions between the mamillary bodies and the third nerve in cats produce states of somnolence, exaggerated muscle tonus of a plastic type and

certain reactions which are found in such states as catatonia and encephalitis. These facts are somewhat related.

Dr. Melvin W. Thorner: Almost invariably, when one speaks about these drugs some one brings up the question, "Of just how much value are they practically?" I do not know whether sodium amytal alone has ever resulted in cure. It is a therapeutic aid at times, but at the present stage one thinks more in terms of what these agents do rather than of what value they are going to be therapeutically. I believe with Dr. Appel that they will be of value in clarifying the psychologic structure of psychoses.

Dr. Appel mentioned the use of bulbocapnine. Bulbocapnine produces in dogs and cats a state resembling catatonia. This state is released by the injection of sodium amytal in the same animals. Since sodium amytal is antagonistic to some of the manifestations of catatonia, some writers have educed this bit of evidence as showing that the state produced by bulbocapnine is similar to the catatonic state. To my knowledge no one has given bulbocapnine to persons who are not catatonic.

Continuous psychotherapy associated with the administration of sodium amytal has been used, but not extensively. My impression is that sodium amytal is of little help in the case of an inaccessible patient, except to render him momentarily accessible. When the effect of sodium amytal wears off, the patient relapses and the symptoms usually return.

Dr. Palmer's results and those of many other investigators indicate that prolonged narcosis in cases of manic-depressive psychosis is of value. It is important to remember that when one speaks of the action of the drug one must think closely of concentration or dosage. When one obtains what appears to be the opposite of a release of inhibition, as in cases of marked depression, usually the dose has been more than that necessary for the release of inhibition in catatonic states. The question of dosage is important. With regard to stupor and catatonia, many depressed patients with manic-depressive psychosis who become stuporous act as catatonic patients do under the influence of sodium amytal. They become more communicative, and one senses more emotional rapport; if they have been mute before they may speak to the physician.

Snap-Shot Diagnosis and Experimental Study of the Accuracy of Diagnosis in Brief Examination of Psychiatric Patients. Dr. Edward A. Strecker and Dr. Lauren H. Smith.

One hundred patients, both male and female, were submitted to an especially short and limited examination to ascertain how accurate such short examinations may be under circumstances usually encountered in wards in a psychopathic department of a hospital. The examination was divided into two parts: (1) objective, consisting of inspection and neurologic tests of pupillary action and knee jerks and (2) subjective, consisting of the following three questions: "Why did you come here?" "How do you feel?" "Tell me your story." No other facts were known about the patient. On the basis of this examination, a diagnosis was made, and the diagnoses were checked against those made at the time of the patient's discharge from the hospital or against those made at hospitals to which the patients were transferred. Accuracy of approximately 60 per cent was found to exist. The study was planned as an experiment, and the procedure is not recommended, but the results show that a certain degree of accuracy exists even under such a limited and incomplete type of approach.

DISCUSSION

Dr. Baldwin L. Keyes: It is surprising that 60 per cent accuracy in diagnosis was obtained. One is accustomed to walk through the wards of the Philadelphia General Hospital and say, "That is such and such." If one stops for five minutes and makes a 60 per cent accurate diagnosis, it should encourage one to stay at least that long. The fact that it takes ten days to bring the accuracy up to 80 per cent is discouraging; in private practice one can probably secure in two hours

the information which it may take ten days to accumulate at Blockley. The success of the observation period of several weeks at the Philadelphia General Hospital emphasized the wisdom of the old policy of holding to a four week period of observation before considering a diagnosis accurate.

DR. W. COLE DAVIS: Dr. Smith seemed to assume that 100 per cent accuracy is secured under prolonged observation. That is erroneous, and hence perhaps a percentage based on the accuracy of diagnosis after long observation would be better. I saw a patient a few days ago in the Northfield Hospital who had wandered from one hospital to another in Pennsylvania, New Jersey and New York. About five diagnoses were made; one neurologist diagnosed the condition schizophrenia once and as manic-depressive psychosis the next time. Physicians do not agree even with themselves after long observation.

DR. R. S. BOOKHAMMER: At the Philadelphia Hospital for Mental Disease diagnoses are not considered 100 per cent correct by any means, but when I saw the program I looked up some cases and found that since 1932 dementia paralytica had been wrongly diagnosed in 23 cases at the Philadelphia General Hospital. In 18 it was diagnosed as senile psychosis, in 2 as psychosis with cerebral arteriosclerosis, in 1 as manic-depressive psychosis, manic type, and in 1 as psychosis secondary to cerebral thrombosis. The average age of the patients was 67. A correct diagnosis would have been made in every case if a serologic examination of the spinal fluid had been made. The services from which these patients came were fairly evenly divided between the various chiefs.

DR. BERNARD J. ALPERS: I wish to ask Dr. Smith what the conditions thought to be manic-depressive psychosis and schizophrenia were found to be when they were rightly classified.

DR. FREDERIC H. LEAVITT: Dr. Smith's attack is interesting but is dangerous. It is important to teach resident physicians at the Philadelphia General Hospital how to take histories and to arrive at conclusions from the material available. It is dangerous to put down on a chart what one may think of a case after five minutes of observation. It is better to make the study for five minutes but not to put down anything on the chart until the patient has been observed for ten days. That is more important than a snap-shot diagnosis.

DR. ROBERT A. MATTHEWS: Dr. Smith has given the psychiatrists at the Philadelphia Hospital for Mental Diseases too much credit for correct diagnoses. Perhaps if he saw patients now in whose cases their diagnosis differed from his, he would agree with the original diagnosis and disagree with theirs. Dr. Alpers asked what the correct diagnosis was in these cases of manic-depressive psychosis. Sometimes they turned out to be cases of catatonic excitement which, under a short period of observation, is difficult to differentiate from manic-depressive psychosis of the manic type, especially when a complete history is lacking. There is a psychotic reaction, most common in Negroes, which for want of a better name is called colloquially "Lombard Street psychosis." In these cases there are often a number of etiologic agents involved: psychologic factors, toxic-exhaustive features and alcoholism, which make it difficult to know what is going to happen even after observation for ten days.

DR. JOSEPH C. YASKIN: My first basic training was secured under a man who could make a good examination within ten mintues. I took his example too seriously, followed it in one case and ordered the discharge of a man who had created a scene in a hotel in New York. I said: "He is sane; there is nothing the matter with him." They said: "All right, but if he comes back. . . ." He came back in an ambulance under police surveillance, and Dr. Gregory was called. He said to me: "You can examine a man, as I do, in ten minutes, but do not give an opinion for ten days." My own feeling in the matter is that one is not justified in basing an opinion on a brief examination, certainly not in the training of interns, and not as a basis for treatment and prognosis. In order to make a prognosis, one must know more than the mere stated classification of type of psychosis.

One is not dealing any longer with manic-depressive reactions and schizophrenic reactions, but with the reaction of the personality as a whole.

DR. LAUREN H. SMITH: Dr. Matthews has answered Dr. Alpers to the point. Many conditions of mania instead of being "manic-depressive, mixed" or "manic-depressive" have turned out to be schizophrenia. As regards the so-called "Lombard Street psychosis," I certainly find it difficult to find out whether an active Negro is really manic or merely excited. This short method of examination was worked out as an experimental study. This is the type of examination every one must make at times. It is dangerous, however, to make rounds of the wards and then make a diagnosis on such scanty data. The diagnosis thus made depends in part on how one feels; it depends in part on one's own introversion or extroversion. I have a habit in making rounds of putting down impressions and usually two or three possible classifications. It is highly dangerous, one can see, to make a snap-shot diagnosis in five minutes, for in that length of time one cannot make an accurate study. Yet one can feel that one has at least a 50 per cent basis of accuracy. A real diagnosis can come only after days of continued observation and study have proved or disproved certain first impressions.

LOS ANGELES SOCIETY OF NEUROLOGY AND PSYCHIATRY

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LEO J. ADELSTEIN, M.D., *President, in the Chair*

SYMPOSIUM ON THE POSTCONCUSSION SYNDROME

PRESENTATION OF A CASE OF POSTCONCUSSION SYNDROME. DR. ARTHUR R. TIMME.

A married woman, aged 39, received a blow across the vertex. There was some laceration of the scalp but no fracture. The fact of unconsciousness cannot be determined, as she was alone at the time and does not remember whether she was unconscious or not. She remembers the blow and getting up from the ground and going to seek help, but she does not remember the interval between those two occurrences. She was an extrovert type of person, making friends easily. She enjoyed a rather happy married life and was interested in athletics. There had been some tendency to obesity following salpingectomy in 1918.

About ten days after the injury she began to feel peculiar and unreal. Her husband and closest friends did not seem real to her. Her right hand and arm began to tremble so that she could not write legibly. Speech became slurring and hesitant, and at times resembled a stammer. She became much depressed. For several days she had a temperature of 102 F. in the afternoon, and she still has spontaneous attacks of fever with the temperature as high as 102 F. She became unhappy with her own people and preferred to be with strangers. Although the tremor was on the right side, the left side of the body became strange and peculiar to her. It seemed as though it might belong to a stranger rather than to herself. The whole left side would frequently "go to sleep." The hair on the left side of the scalp would not take a permanent wave and remained lusterless, lifeless and slightly brittle. There developed a "change in character." From happy and easy-going she has become irritable, hypersensitive and crabbed. She is unable to concentrate or integrate an effort in any direction consistently. She has a rather intractable insomnia. When she grieves she says that she feels the grief on the right side of the body and not on the left; for instance, when she saw her dog killed in the street and screamed in fright she felt the fright on the entire right side of the body but not on the left. The left hand and foot always feel colder,

and there are occasional attacks of dizziness and nausea. The husband reports frequent outbreaks of spontaneous weeping for no apparent reason. There is a frequent feeling that the left side of the body is twice as large as the right. Movement of the left arm or leg requires some concentration and voluntary effort, whereas movement of the right side is not so affected. The facial expression has become strained and drawn so that some former friends have difficulty in recognizing her.

The patient is 5 feet and 5½ inches (166.4 cm.) in height and weighs 161 pounds (73 Kg.) (she has been gaining weight since the injury). The cranial nerves are not primarily affected, except that the right retina looks slightly congested; the veins are a little larger than those on the left side, and the disk outline is a little less distinct than on the left. The patient stated: "I do not see two things when I look at one object, but it looks different in each eye." The dynamometer showed the muscular coordination of the right hand to the 45 and that of the left hand 15. There is a coarse tremor of the right hand which is practically constant and an occasional tremor of the head. There is no tremor of the left hand. All tendon reflexes are extremely active, but there are no pathologic reflexes. There is slightly more than normal swaying in the Romberg position. The finger-to-nose and the heel-to-knee test were poorly performed on both sides. There is left hemihypesthesia extending to the midline and involving all mucous membranes within reach. The loss of sensation is not complete, but all forms of superficial and deep sensations are involved. There seems to be a reduction of hearing, smell and taste on the left side, but this is not clearcut.

This case is presented to stimulate discussion and possibly to throw light on some of the findings that have long been labeled hysteria. The hemihypesthesia certainly appears to be of the hysterical type. My impression is that there is some involvement of the right thalamic region. This would account for the tremor on the right, the unilateral involvement of the emotional centers, described by Cushing and others, and the emotional and sensorial differences between the two sides of the body. Practically every sensation on one side of the body encounters a cell station in the thalamus of the opposite side. In this case the point that seems to localize the disturbance in the right side of the thalamus, namely, the motor signs, the spontaneous fever, the spontaneous weeping, the emotional differences, etc., may indicate that the usual typical hemihypesthesia has some physical basis in the thalamus.

PRESENTATION OF A CASE OF POSTTRAUMATIC PSYCHOSIS WITH MENTAL DETERIORATION. DR. CULLEN WARD IRISH.

A man aged 37 was injured on Aug. 17, 1933, at 3:45 p. m., when he was struck by an automobile. He immediately became unconscious and had not regained consciousness the next afternoon at 3:30, when he was examined by Dr. Carl Rand. He had a fracture of the left clavicle, two lacerations of the scalp in the left frontotemporal area, 3 and 1 cm. in length, respectively, and a hematoma of the left side of the scalp. No depressions were noted. There was swelling and discoloration about the left eye, and the entire left side of the face was swollen. The pupils were of medium size, regular and mobile to light. The right ocular fundus was normal; the left was not seen. There were no bleeding from the ear and no paralysis. No abdominal reflex was present. The knee and achilles tendon reflexes were equally sluggish, if present at all. A bilateral Babinski sign was elicited, but no Oppenheim or Gordon sign or ankle clonus. The patient's temperature ranged between 100.6 and 101.4 F., and the pulse rate between 60 and 76. The blood pressure was 125 systolic and 65 diastolic. The neck was stiff, and a moderate bilateral Kernig reaction was elicited.

On December 5, the patient was confused and distractible and talked about events which had occurred twenty years before. He had hallucinations and delusions and cursed fellow passengers on street cars.

Neurologic examination revealed normal disks. The pupils were equally sluggish. The Romberg test was negative, and strength was normal. There

was no incoordination. The reflexes were normal. A Babinski sign was present on the right, but there was no ankle clonus. Roentgenograms revealed a fracture of the left frontal region. Blood tests gave negative results. The symptoms presented were entirely mental.

On December 14, a neuropsychiatric examination revealed: dilated pupils which reacted slowly through a small arc to light, with hippus; stronger biceps and triceps reflexes on the right than on the left; a decreased knee jerk on the left; abnormally plantar-flexed toes, and absence of abdominal and cremasteric reflexes. The patient was distractible and disoriented and presented marked impairment of memory; all his past activities were placed in Paris. There was much confusion and no accurate general knowledge or knowledge of family history. He said repeatedly: "Oh, it's terrible." He had hallucinations regarding the presence of animals in the room, etc., and could not name his nurse.

On Feb. 5, 1934, the patient was careless about personal appearance; he had to be shaved, dressed and undressed and offered some resistance to bathing. He did no reading, but sat idly, talking constantly and extremely distractibly. On March 16, it was noted that he misused words and used neologisms, such as "simultaneously speaking politically," "detrimentally speaking," "preloaded him out, externeously" and "I am undormitory." At a picture show he was disinterested, retaining no memory of the plot, players, etc. He was hypercritical, with some irritability and argumentativeness present. On April 3, some improvement in memory was shown, with less confusion. The patient mentioned eastern cities, but was disoriented. He resisted being taken for walks. Throughout April he continued to remain unoccupied and resisted going out, dressing, bathing, etc. He had no remembrance regarding picture shows, food, etc. He gave some episodes which occurred on the east coast distractibly, illogically and with no elaboration.

In the last two weeks of May the patient remembered eastern cities, localities, highways and approximate distances between cities and locations. He still placed many activities in Paris and resisted dressing, bathing, etc. By July 17, he was walking about the grounds unaccompanied. He rarely used neologisms and was approximately oriented as to the place and attendants. By August 27, he was completely oriented and knew approximate distances. He did not know how long he had been in California. He could do the simplest arithmetic and had some insight into his condition. By October 30 he had walked ½ mile (about 805 meters) to the village for several weeks. He read headlines and some news items. Improvement in memory was noted. On December 17 minor episodes in his past were recited, and activities were no longer placed in Paris. He remembered previous positions and an aunt and a brother; this constituted his entire memory. He used his radio, puerilely. By Feb. 28, 1935, he was able to give bits of history logically, but little elaborated. He stated that he was never in the army or outside the United States. He did nothing except take walks, but dressed, bathed himself and read; he evidenced mental deterioration in the form of poor associative processes, impaired memory, absence of planning or concern regarding the future, limited elaboration, marked lack of initiative, poor judgment and general impairment of cerebration.

No involvement was shown on neurologic examination and little from a superficial mental examination. One thing the patient told me this evening as I was trying to refresh his memory about past activities before he came to California demonstrated his trend of thought, distractibility, failure of proper association and elaboration. [The patient's mental state was demonstrated to the members of the society, as shown by the answers published at the end of this presentation.]

The acute psychotic manifestations have subsided, but little change has been shown in the mental condition during the past three months. The patient has never shown incoordination or ataxia or complained of vertigo or headache. Minor involvement of the pyramidal tract was shown for a few weeks after the accident, but for over a year no neurologic signs have been elicited. The degree of improvement to be expected from the present state of mental deterioration shown is problematic.

Dr. Irish: "Will you please tell us again, a good deal as you told me, what happened to your father to bring about his death?"

Answer: "Well, the only thing I could say—that he died in Oklahoma some years ago, and he had been sick some—over quite a while—and then the doctor sent him away, and he went away for quite some time. Then he came back, and he was called in the morning, and mother and I were staying at the house, and he died that day. I don't have much of a family life. I have a brother in Oklahoma, and I have two aunts, two uncles, and two of the last who are left."

Dr. Irish: "How long have you been out here?"

Answer: "Well, I am here around, say, seven or eight years, no, more than eight years. I worked for the company quite a while, and I have been here about a year and a half or two years, and then I went back to the Paraffine Company."

Dr. Irish: "How do you think your mind works?"

Answer: "My mind is much better than then."

PRESENTATION OF A CASE OF POSTCONCUSSION SYNDROME WITH ENCEPHALOGRAMS. DR. EUGENE ZISKIND.

I also wish to report a case of traumatic psychosis which has several features of special interest. The patient, a man aged 26, was brought by his mother because of unusual behavior. His manner was surly and belligerent. All of his answers were "Oh yes!" "Oh no," "I guess so," and there was no spontaneous speech. The story was that the patient had lost his position three years previously and since then had stayed about the house most of the time, doing nothing. His behavior at home was much as I have described. The mental status was not determined. General and neurologic examinations together with routine laboratory tests failed to reveal any pertinent abnormalities.

The patient was given sodium amytal intravenously; immediately there was a change in attitude. He became amiable, affable and cooperative and even somewhat elated. He then spoke in complete sentences. He told the following story: Five years previously he had become involved in a fight in a house of prostitution. His head was seized and banged against the wall several times and his upper front teeth were knocked out. The family did not know of this episode but recalled that the patient at that time gave up many of his previous interests and companions, presumably owing to embarrassment over having lost his front teeth. Under the effects of this drug it was possible to determine that the patient had a Korsakoff syndrome. He soon lapsed back to the previous state.

With subsequent injections of sodium amytal it was possible to perform an examination of the spinal fluid and encephalography, after 155 cc. of spinal fluid was replaced by air. The pictures showed enlargement of the subarachnoid spaces over the vertex. Incidentally, the patient's attitude has changed to that observed previously when sodium amytal was administered. The organic deficiency is still present. This case is of interest primarily in that (1) a history was obtained with the patient under the influence of sodium amytal which could not otherwise be ascertained and (2) encephalographic evidence of atrophy of the brain was demonstrated. Traumatic psychoses are not common, and those in which encephalography indicates loss of brain tissue have been infrequently reported.

I wish to make one observation in regard to the discussion on the postconcussion syndrome. One frequently sees such conditions diagnosed from a good neurologic examination without psychiatric investigation, and vice versa. Undoubtedly there will be problems which in the present state of knowledge cannot be absolutely settled in some cases. Nevertheless, I believe that it is inexcusable not to perform both types of examination in every case.

THE POSTCONCUSSION SYNDROME FROM A NEUROPSYCHIATRIC POINT OF VIEW. DR. J. N. NIELSEN.

Reverting to the chairman's remarks about the question whether cerebral concussion is an organic or a functional condition, I note that there is usually more than one factor in the case, and frequently there are three. There is the evidence of organic injury to the brain; there is a functional disturbance due to the diffuse

organic pathologic process, and there may be a psychoneurosis superimposed on this as an unconscious effort to obtain more compensation.

It is difficult indeed for even the conscientious examiner to maintain an unbiased point of view. If a physician sees a patient who wishes to have his case opened before the Industrial Accident Commission, there is a tendency to see the patient's side of the question. If an insurance company sends the patient in, there is a tendency for the physician to underrate the patient's case. Perhaps the most satisfactory arrangement is to see the patient for the Industrial Accident Commission. Besides this factor, some physicians have certain constant leanings. There are those who consider neurosis in a class with malingering and only grudgingly acknowledge that a patient may have a psychoneurosis. There are others who tend to see a psychoneurosis even in frank malingering.

It seems to me that the only way in which all can arrive at the same point of view is to be willing to start at the same place and see the same thing. At the General Hospital Dr. Courville has a large collection of brains from persons who had cerebral concussion but later died of something entirely unrelated. In these brains there are large organic defects, in spite of which the patients returned to their work. If the patient has been unconscious for more than three hours there is practically always permanent evidence of the injury in the form of contusions and hemorrhages. Physicians who take the attitude that patients who complain of the residuals of cerebral concussion have compensation neuroses would do well to examine this material. They would probably never again claim that the patient had not been injured.

I distinctly recall 3 cases in which there was no litigation neurosis because there was no element of compensation in the case. One was the case of a Jewish woman who was injured while driving a car. She carried no insurance and was not held liable for damage to the other car. She explained to me in detail that there was no use discussing any legal side to the question because nothing could possibly come up, yet she complained of dizziness, headache and emotional instability and found it impossible during an entire year to hold a position. She had been unconscious for a short time and obviously suffered from concussion, but not from litigation neurosis.

In another case a rancher had similarly been in an automobile accident but had collected damages. He presented a case that was entirely free from any legal side. Yet he had completely lost his sense of direction, could not identify roads that he had traveled many times, could not recognize people that he formerly had known and lost his tools even when they were right before him. He always took his wife with him when he drove anywhere because while he could handle the car mechanically he did not know when to turn or in which direction to turn unless she told him.

The third case, in which the legal matter was settled, was that of a man who was awarded about $8,000. His wife had been told that his symptoms would disappear as soon as the suit was settled. It was settled out of court, but the patient still was unable to work and had staggering spells, dizziness and periods of impulsive activity. He had a complete change of personality and could not be left alone at home. His wife at times would leave him with the neighbors, but on one occasion he attempted a sexual assault on a woman whom he had known for years and who was a friend of the family. It was only by the timely return of his wife that a calamity was averted.

I am offering these cases to show that changes of personality, which the patient himself cannot explain and which the physician examining him cannot establish without consulting relatives, certainly occur not infrequently as a result of cerebral concussion entirely apart from litigation neurosis.

THE NEUROLOGIC ASPECTS OF THE POSTCONCUSSION SYNDROME. DR. CARL W. RAND.

True posttraumatic psychosis in my experience has been extremely rare. I recall having seen only 2 cases. The psychosis in the first case appeared shortly

after a severe fracture of the skull and subdural hemorrhage. The patient, a man, has been institutionalized for the past ten years and, I am informed, shows very little change at present. The second is the case presented by Dr. Irish.

I have long been impressed by the fact that children under the age of puberty are unusually free from posttraumatic neuroses. They probably have very much the same pathologic process, from the standpoint of organic changes in the brain, as adults. This lack of postconcussion syndrome, it seems to me, is significant and may be taken as evidence of the psychogenic origin of some of the symptoms in adults.

THE PATHOLOGIC PROCESS OF CEREBRAL CONCUSSION. DR. CYRIL B. COURVILLE.

The term "postconcussion syndrome" refers to the particular symptom complex which so frequently follows injury to the head, characterized by recurrent headaches associated with dizziness and by variable degrees of emotional and mental disturbances. The findings on neurologic examination are usually not marked and may be absent altogether. There is no correspondence between the severity of the injury and the intensity of the symptoms. For example, a very severe injury may be found with very few or no symptoms of this sort, particularly if the patient was properly treated during the acute and subacute stages of the condition. On the other hand, a relatively minor injury which had dazed the patient only for a short interval may result in long continued symptoms. The nature and extent of localizing signs depend more definitely on the severity and nature of the injury.

Since it is not possible to make a direct study of the altered mechanism which is responsible for symptoms of this syndrome, a concept of the pathologic process of concussion must be gained from other sources. One may secure some information as to the nature of the process from an analysis of the clinical history itself. One may also obtain some information from a study of the changes in the pressure and character of the spinal fluid. From a purely pathologic standpoint knowledge is derived as to the possible responsible lesion in cases of concussion from an examination of the cerebral cortex following minor injury, the patient having died from some other coincident injury.

Another way in which one may gain some conception of the character of minor lesions which may be survived is by a study of the brains of persons who have sustained an injury to the head in former years and have survived for a variable period, death being due to some other and often unrelated condition. In the Cajal Laboratory of the Los Angeles County General Hospital I have had an opportunity to study clinically about 30 cases of old injury, and the findings in these cases have been illuminating.

In order to appreciate fully the possible mechanism of concussion, it is necessary to know that two definite processes are initiated by injuries to the head. The first of these is a disturbance of function, affecting predominantly the nerve cells and blood vessels. The commotional disturbance of nerve cells is evidently responsible for unconsciousness, and the duration of coma may be taken as a direct indication of the severity of injury to these cells. This, however, as previously stated, is of little moment in any analysis of the problem of concussion. It is likely that the disturbance of the vasomotor control of blood vessels is of far greater significance in an understanding of the nature and character of the so-called postconcussion syndrome. The shock of the injury is no doubt followed by a derangement of the vasomotor mechanism of the cerebral and meningeal vessels, so that more fluid escapes from the small vessels and capillaries into the perivascular spaces and the subarachnoid space and ventricles (via the choroid plexus and ependyma). This increased transudation of fluid is loosely spoken of as "cerebral edema" but is more accurately known as the "wet brain" of the neurosurgeon, who has the opportunity to examine the surface of the brain during life. Cerebral edema in a specific sense refers to the fluid which lies within the cerebral tissue itself and therefore is not in direct communication with the perivascular fluid spaces.

This altered balance between the blood serum on one hand and the cerebrospinal fluid on the other undoubtedly continues to exist for long periods of time in

many instances. This is evidenced by the increased pressure of the spinal fluid, which may persist for weeks or months after the original injury. While the increase in the pressure and amount of spinal fluid is anatomic evidence of disturbance of the vasomotor control, the patient experiences this instability subjectively by the bouts of headache, dizziness, mental fogginess and, at times, emotional disturbances. When long continued, this disturbed balance results in enlargement of perivascular spaces and of the subarachnoid space and ventricles, a change which can be observed in the brains of persons who die months or years after an injury to the brain.

The second process which is initiated by the injury depends on the mechanism of the injury and the severity of its force. It is manifested by the alterations in architecture of the brain and in the structure of the various cellular elements. The effects are found in the intracranial hemorrhages and contusions which are so common in patients who have been unconscious for more than two or three hours. These gross contusions may be responsible in some instances for some of the psychic symptoms which these patients manifest. In addition to the gross lesions, petechial hemorrhages in the white substance of the brain, microscopic focal hemorrhages and areas of necrosis, *Herde,* which are sometimes present may play an important rôle in the emotional and mental disturbances that are so frequent in these cases.

The exact relationship between morphologic changes in the brain and the symptoms following concussion has never been satisfactorily worked out. It is obvious that symptoms which are transient and tend to recur at intervals, such as headaches and dizziness, are more likely evidence of an alteration of function than of structure and are not to be explained by changes in cerebral tissues. On the other hand, one would expect that symptoms resulting from architectonic changes would more likely be of more constant and permanent character. An analysis of the so-called postconcussion syndrome from a pathologic standpoint would lead one to believe, therefore, that the headaches and vertigo and perhaps in part the variable degree of emotional and psychic disturbances are the result of a disturbed vasomotor control of the dural and cerebral vessels. More likely those more permanent and long continued symptoms and signs which follow severe injury to the head are to be explained on the basis of gross or microscopic cortical or medullary lesions.

In addition to symptoms which are to be explained on the basis either of disturbed physiology or of altered structure, it is necessary to remember that every patient reacts to his injury in his own peculiar manner, both mentally and emotionally. This reaction depends to a considerable extent on the patient's psychic background and experience. It also depends on circumstances which may arise *after* the accident, such as the possibility of gaining compensation. In analyzing a given case, this individual reaction must be taken into consideration.

In conclusion, therefore, it may be said that three factors must be thought of in evaluating the manifestations of the postconcussion syndrome: (1) disturbance of the cerebrospinal fluid-blood serum balance; (2) the possible presence of gross or microscopic organic lesions of the brain and (3) the patient's particular mental and emotional reaction to the injury. Intelligent analysis in a given case of necessity includes a consideration of all three, and the proper evaluation set on each will aid one in arriving at an approximate conclusion.

THE POSTCONCUSSION SYNDROME: COMMENT. DR. S. D. INGHAM.

The question of the postconcussion syndrome seems to me to be primarily a matter of diagnosis of the entire clinical picture after injury to the head. A bump on the head often causes an organic lesion of the brain, as Dr. Courville has stated, and it may be assumed that there are many cases in which there are indefinite but disabling symptoms as a result of diffuse injuries. On the other hand, persons who have had accidents without receiving injuries to the head also have disabling symptoms which may be ascribed to psychoneurosis. So in making

the diagnosis one must consider both the organic and the psychologic factors and try to evaluate each. All who have dealt with these cases will probably agree that most patients who have had severe injuries to the head present a mixture of symptoms, some of which are the direct result of physical damage to the brain and some of which are not directly related to the traumatism. It will also be agreed that the prospect of compensation or some other benefit is often a potent factor in the development and persistence of symptoms. One other important factor of the symptomatology in these cases is the shock reaction due to the experience of the accident and not to the traumatism. Many persons who go through railway or automobile wrecks or earthquakes without physical injuries are sensitized to anxiety and fear reactions, which may persist indefinitely. A woman was in an automobile accident in which the automobile turned over. She received only minor bruises and no concussion or injury to the head, and there was no benefit motive. For a year following there were gradually diminished physical as well as anxiety symptoms every time she rode in an automobile. Each automobile ride caused an exaggerated fear reaction with concomitant pallor, sweat, nausea, rapid pulse and general physical distress. In many patients who receive injuries to the head this factor of fear sensitization complicates the picture.

In addition to the shock reaction and the benefit motive, other psychogenic factors enter the problem, such as enforced idleness, economic worries, the conviction that injuries are permanent, defense reactions and antagonisms in patients who believe that they are not understood or that they are not being treated fairly. In many insurance and industrial accident cases the patient states that he has been accused of insincerity, and the reaction is an increase in the psychoneurotic symptoms. By the time they come to the neurologist many patients have been examined and treated by a number of physicians without benefit but with relatively fixed psychoneuroses which might have been avoided.

In the postconcussion syndrome, therefore, there is a triad of symptoms: those due to organic changes, those due to the primary emotional shock and those developing after the injury as a secondary psychoneurosis.

The symptoms of brain trauma per se may be classified into focal and general, general symptoms constituting a large part of the true postconcussion syndrome. There is some reason to assume that severe, jarring blows on the head followed by prolonged loss of consciousness cause diffuse pathologic changes in the brain, manifested by marked general and no focal symptoms. In such cases it is difficult to differentiate the organic and the psychologic factors. A professional man was injured in the earthquake two years ago in Long Beach. Falling bricks from a building buried the automobile in which he was sitting. He was unconscious for several days but apparently recovered from the bruises in three or four weeks and returned to his office. There was no question of insurance, no one to sue and no benefit to be gained by the disability. For two years, however, he has been unable to make the simplest social adjustments. Formerly a successful, alert, sociable man, he has become a recluse, never reads the paper, is irritable and emotionally unstable and retires to a back room when friends come to his home for dinner. Neurologic examination shows no evidence of a gross lesion of the brain, and his condition has been diagnosed as a postconcussion syndrome.

The technic of neurologic examination is not sufficient to make a complete diagnosis of injury to the brain, but changes in personal habits or personality as a whole, considered from the psychiatric standpoint, may prove to be a valuable means of diagnosing diffuse injuries of the brain. It is a mistake to ascribe all of the vague symptoms following trauma to the head to psychoneurosis. It is also a mistake to ascribe all symptoms of psychoneurosis to a desire for compensation. The psychiatric approach may be a valuable help in the diagnosis of organic disease of the brain through the study of personality reactions, habits and emotions and analysis of the patient's ability to adjust himself to his environment and also in determining in what degree the motive for gain or other psychologic factors are operative.

THE PSYCHIATRIC ASPECTS OF THE POSTCONCUSSION SYNDROME. DR. AARON J. ROSANOFF.

From my experience I am able to confirm Dr. Ziskind's statement to the effect that in many cases the neurologic work has been thoroughly and competently done but the psychiatric phase has been neglected. The psychiatric investigation is of special importance in cases in which the question arises as to whether there has been a physical damage or the condition is purely mental. Neurologic methods, including encephalography, are not adequate to reveal physical damage in all cases. In other words, the fact, in itself, of negative neurologic findings cannot be depended on definitely to exclude physical damage; it would not justify the diagnosis of hysteria, malingering or whatever one wishes to call the "nervous" conditions in which no physical damage has occurred. For such a diagnosis it is necessary, in addition to the negative neurologic findings, to produce positive demonstration of the underlying motivation, together with other features of the psychogenic mechanism. Such demonstration can be accomplished only by a systematic psychiatric investigation of character, temperament and personality; various situations preceding, accompanying and following the accident; the mental features of the disability, etc. One more point. In the patient, his relatives and friends and his attorney one may expect to find often a mental or emotional bias; but the physician must approach the case in a frame of mind which is free from bias, for the presence of bias, whether for or against, and whether conscious or unconscious, is the principal source of serious error in such cases.

THE POSTCONCUSSION SYNDROME: COMMENT. DR. PAUL E. BOWERS.

Because a patient may have sustained an injury to the head, great or small, and there develop mental or nervous symptoms, or both, it does not necessarily follow that these subsequent symptoms are the product of the injury (*post hoc ergo propter hoc*). The fact that symptoms have, in point of time, been observed following an injury has led some to reason loosely and illogically. One sometimes misconstrues the doctrine of proximate cause. At one time malarial fever was erroneously termed "swamp fever," but when it was learned that the so-called "swamp fever" was really "malarial fever," was due to Plasmodium malariae of Laveran and was transmitted by a certain kind of mosquito and that the victim did not have to live near a swamp in order to get this disease, then the name "swamp fever" was relegated to the limbo of medical mistakes.

During the World War, and for a few years afterward, the blanket term of "shell shock" was applied to all nervous and mental troubles suffered by soldiers, irrespective of the real medical facts at issue. As "charity covers a multitude of sins," so the term "shell shock" covered a multitude of errors in diagnosis. The majority of the persons who developed states of so-called "shell shock" were soldiers who suffered with a fear complex. This mental phenomenon was observed in the soldiers who were not at the front but who were expecting to be called. Soldiers who were prisoners of war and who were interned in the zone of the theater of operations did not present the so-called "shell shock" neurosis; for them the war had ended.

Some day the term "postconcussion syndrome" will be discarded. It has been carelessly and indiscriminately applied to all sorts of mental and nervous states following head injuries, severe or trivial. In some instances this blanket and unscientific label has been applied to mental and nervous symptoms which existed before the injury but which have been charged to the injury for the purpose of gain.

Book Reviews

Die psychiatrischen Aufgaben bei der Ausführung des Gesetzes zur Verhütung erbkranken Nachwuchses. With an appendix: **Die Technik der Unfruchtbarmachung.** Edited by K. Bonhoeffer. Price, 3 marks. Pp. 98. Berlin: S. Karger, 1934.

This small book is composed of brief lectures delivered at the neuropsychiatric clinic of the Charité Hospital in Berlin. These lectures are intended to aid psychiatrists and neurologists in coming to decisions about sterilization in accordance with the new National Socialist laws. The subjects covered are feeblemindedness, schizophrenia, manic-depressive psychosis, epilepsy, heredodegenerative nervous diseases and alcoholism. A final chapter deals with the technic of sterilization. The fact is stressed that in sterilization of women a laparotomy is always necessary.

All the lectures are rather sketchy, and they have little scientific or practical interest. Despite the efforts of the authors, the inadequacy of present knowledge concerning the rôle played by the hereditary factor in neuropsychiatric diseases and the difficulties involved in its utilization for their prevention become apparent. As a matter of fact, the problems of the heredity of mental disease are so difficult that it is perhaps not a bad idea of the German government to settle them by statutory law. But such a procedure has nothing to do with science. Well nigh classic is the order of the Berlin City Government, twice quoted here: "When an exogenic cause is not demonstrable . . . feeblemindedness has to be regarded as hereditary in the sense of the law." The general impression that this book leaves with the reader is one of a group of academic teachers performing a law-enforced psychiatric goose-step.

Psychology and Psychotherapy. By William Brown, D.M., D.Sc., F.R.C.P. Third edition. Price, $4.75. Pp. 252. Baltimore: William Wood & Company, 1934.

The third edition of this interesting book contains much material for serious study and consideration. The author is well known in the fields of psychology and psychiatry, particularly in England.

In this presentation, in the words of Brown, his "approach to psychology has been through mathematics, and statistics, philosophy and then medicine in its various branches. . . . Years of analytical and other forms of clinical work in medical psychology since . . . have brought me to the view which this book represents." The emphasis is on the relation of psychology and psychotherapy in clinical work and in the theoretical consideration of an integrated working of mind and body. Freud's theories and contributions are discussed at great length, but other contributions as well are given deserved recognition. Although a philosophic trend continues through many of the chapters, the material is related to practical things of everyday life as seen in patients and in the experience of psychiatrists.

In the appendix examples of cases of neuroses seen in the wards are cited. An interesting account by a patient of his psychoanalysis and some mathematical computations regarding a central intelligence factor are given. The book is well indexed. It is an interesting reference book for graduate students but is not suitable for undergraduates or lay readers.

Hallucinations et délire: Les formes hallucinatoires de l'automatisme verbal. By Henri Ey. Preface by J. Séglas. Price, 15 francs. Pp. 192. Paris: Félix Alcan, 1934.

In a preface to this book Séglas briefly summarizes his various well known studies on hallucinations, published in the period between 1888 and 1914. The presentation by Ey is derived to a large extent from Séglas.

Ey stresses the intimate connection between hallucinations and delusions. He deals almost exclusively with auditory hallucinations and discusses their relationship to passivity, influence, possession, depersonalization and other phenomena. This forms the subject matter of a great deal of recent French psychiatric literature. Ey takes a stand against the too mechanistic and simple explanations of "automatism." He believes that "delusions of influence" and verbal psychomotor phenomena which often accompany them occur not only on an "organic" basis, as the result of an automatism, but also on a psychogenic affective basis. The whole discussion is rather formal and lacks clarity, especially in those parts which are most closely related to clinical observation. The book presupposes a knowledge of French psychiatric literature, which may detract from its value for the average reader.

Grundriss der Kurzwellentherapie: Physik-Tecknik-Indikationen. By Dr. Ing. Wolfgang Holzer and Dr. Med. Eugen Weissenberg. Price, 8 marks. Pp. 189, with 53 illustrations and 9 tables. Vienna: Wilhelm Maudrich, 1935.

This book serves as an introduction to the use of short-wave electricity in medicine and biology and deals with physics and technic. In an effort to avoid some of the failures of therapy the basic physical aspects have been discussed in detail. This type of therapy, according to Holzer and Weissenberg, has a large field, being applied in dysfunction and diseases of almost every organ in the body. The authors emphasize that the book is a groundwork and is not claimed to be complete or contain an exhaustive review of the literature. References to the literature have been made in specific instances of practical value. Finally the points of view as to the choice of apparatus are discussed. Chapter 14 deals particularly with diseases of the nervous system and the efficacy of this type of therapy in the handling of various conditions, such as disturbances of motility and sensation, multiple sclerosis, syringomyelia and psychoses.

Bildung und Ausbildung beim schweizerischen Pflegepersonal für Gemüts- und Geisteskranke. By W. Morgenthaler. **Heft 7. Personal- und Anstaltsfragen.** Price, 2.30 francs. Pp. 47. Bern: Hans Huber, 1934.

This brochure should be of interest to all those who are in any way responsible for the planning and administration of the nursing care of patients with mental disease. Morgenthaler gives a brief history of the establishment of regular training courses for nurses in Switzerland. He discusses the general principles and the question of examinations and diplomas. He does not omit pointing out the resistance that he has encountered in his own efforts, chiefly on the part of older psychiatric colleagues in state hospitals.

Since 1927 regular examinations of nurses for persons with mental disease have been held in Switzerland. By 1933 there were only six state hospitals of thirty-five that did not send candidates to those examinations for diplomas. The whole movement is evidently still in a stage of growth and adjustment. Though the discussion applies directly only to the Swiss scene, there is a great deal in this brochure that has universal applicability.

The New Field of Psychology. By Madison Bentley. Price, $3. Pp. 427, with 51 illustrations. New York: D. Appleton-Century Company, Inc., 1934.

This is presented as an introductory book and covers the topics usually included in a first text of general psychology. It would, however, be a difficult book for most beginners to use. Bentley attempts to avoid any assumption of mental states or processes, condemning these as "short-cuts through allegory." His approach to the subject and his discussions of apprehending, executing, inspecting, comprehending and elaborating as "psychological functions" would probably be unnecessarily involved for the beginning student, but they will interest the psychologist who is following the development of psychologic theory.

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